Moderate Prosthesis-Patient Mismatch May Be Negligible in Elderly Patients Undergoing Conventional Aortic Valve Replacement for Aortic Stenosis

Tadashi Kitamura, MD, Shinzo Torii, MD, Naoji Hanayama, MD, Norihiko Oka, MD, Takahiro Tomoyasu, MD, Yusuke Irisawa, MD, Miyuki Shibata, MD, Hidenori Hayashi, MD, Takamichi Inoue, MD, and Kagami Miyaji, MD

Summary

Together with aging of the Japanese population, aortic valve replacement (AVR) for aortic stenosis (AS) is now becoming more and more common in the elderly. When the aortic annulus is too small to allow an adequate sized prosthetic valve, aortic root enlargement is required to avoid prosthesis-patient mismatch (PPM). However, age-related comorbidities including aortic root calcification bring significant risk in performing aortic root enlargement. In the present study, 40 patients aged 75 years or more who underwent AVR for AS were reviewed to determine whether moderate PPM has a negative impact on the long-term results. Operative mortality occurred in 2 patients (5%) and moderate PPM occurred in 8 patients. There was no significant difference in survival between cases with and without PPM ($P = 0.87$). Both aortic pressure gradient (PG) and left ventricular mass index (LVMI) measured by echocardiography were significantly decreased in patients with and without PPM. Reduction of PG was significantly greater in patients with PPM than without PPM ($P = 0.02$). Reduction of LVMI was not different between the groups ($P = 0.58$). Moderate PPM did not negatively influence survival or reduction of PG or LVMI in patients aged 75 years or older who underwent AVR for AS. (Int Heart J 2013; 54: 11-14)

Key words: Cardiac surgery, Outcomes

The proportion of elderly people to the total population is growing in developed countries. In Japan the proportion of people aged 75 years or over was 11% in 2010,$^1$ and it is projected to plateau at over 20 million for some decades.$^2$ Accordingly, an increase in diseases of the elderly has been observed.

Aortic stenosis (AS) is a common disease in the elderly. Otto, et al reported in their population-based prospective study that the prevalence of significant AS in people 65 years of age or older was 2%.$^3$ Therefore, AS is now one of the most common cardiac diseases of the elderly along with coronary artery disease.

When the aortic annulus of a patient undergoing aortic valve replacement (AVR) is too small to allow a prosthetic valve with enough effective orifice area in relation to the body size, aortic root enlargement$^4-^6$ is required to avoid prosthesis-patient mismatch (PPM).$^7$ However, elderly patients often have severe calcification of the aortic annulus and aortic root wall, which brings significant risk in performing aortic root enlargement. Therefore, it is important to assess whether aortic root enlargement is required for each case undergoing AVR.

Although an indexed effective orifice area (EOAI) of a prosthetic aortic valve less than 0.85 cm$^2$/m$^2$ is generally regarded as the threshold for PPM,$^8$ it is still controversial as to whether or not moderate PPM influences long-term survival, especially for the elderly.$^9-^11$ In general, Asians have a smaller body surface area than Westerners. The average body surface area of a Japanese aged 75 years or older was reported to be 1.64 m$^2$ for males and 1.43 m$^2$ for females (http://www.e-stat.go.jp). Therefore, PPM is usually not severe but moderate, if at all. The purpose of the present study was to determine whether moderate PPM has a negative impact on the long-term results of patients aged 75 years or older who undergo conventional AVR for AS.

Methods

Patients: From 1996 to 2011, 202 adult patients underwent a standard AVR for AS at Kitasato University Hospital. Among these patients, 40 who were aged 75 years or older at operation were selected for a detailed analysis, constituting the cohort of this study. The patient medical records were retrospectively reviewed for patient preoperative demographics, diagnosis, hemodynamic and echocardiographic values, surgical procedural data, and outcomes including postoperative echocardiographic data. Preoperative aortic transvalvular pressure gradient (PG) and aortic valve area were measured by cardiac catheterization.
Echocardiographic data were substituted when cardiac catheterization was not performed. The Japan SCORE (https://jaccvsd.hqa.jp/JapanSCORE/JapanSCORE), the Society of Thoracic Surgeons Predicted Risk of Mortality (STS risk score: http://209.220.160.181/STSWebRiskCalc261/), logistic EuroSCORE (http://www.euroscore.org/calc.html), and the EuroSCORE II (http://www.euroscore.org/calc.html) were calculated for each patient based on the preoperative profiles. STS risk score was not calculated for one patient because it was unsupported. The calculated logistic EuroSCORE and EuroSCORE II for patients aged over 90 years were included in the analysis despite their advanced age. An EOAI was calculated for each patient based on the effective prosthetic valve area provided by the manufacturer of the prosthes. An EOAI value between 0.65 and 0.85 cm$^2$/m$^2$ was defined as moderate PPM. Operative mortality was defined as death during hospitalization or within 30 days after surgery. Pre- and postoperative left ventricular mass index (LVMI) was calculated according to the formula of Devereux, et al$^{[22]}$ using echocardiographic data. Pre- and postoperative echocardiographic PG and LVMI were compared within the groups with and without PPM separately, and the regression of LVMI and PG were compared between the groups. The history of recent events and activities of daily life (ADL) were also obtained from the patients and their families by telephone inquiry.

**Operative procedure:** Through a standard full median sternotomy, cardiopulmonary bypass was established using mild systemic hypothermia (32°C to 34°C). Under antegrade and retrograde cardiopulmonary arrest, a transverse aortotomy was created and the aortic valve was replaced with a prosthetic valve in a supra- or para-annular position.

**Postoperative management:** All patients who had a mechanical prosthesis received a regimen of lifelong warfarin potassium for 3 months followed by lifelong low-dose aspirin unless they had other comorbidities requiring warfarin.

**Statistical analysis:** Statistical analysis was performed using JMP 9 software (SAS Institute, Cary, NC, USA). Continuous variables are presented as the mean ± standard deviation. The difference in continuous variables was analyzed using independent sample Student’s t-tests. Categorical variables were compared by $\chi^2$ or Fisher’s exact test according to the type of variables. Survival was analyzed using Kaplan-Meier analysis and comparisons between groups were performed using the log rank test. All $P$ values were two-sided and were considered statistically significant when $P < 0.05$.

## RESULTS

Table I summarizes the preoperative patient characteristics. Mean age was 80 ± 4.2 years (range, 75–91) and 19 patients were in New York Heart Association (NYHA) functional class III or IV. The mean Japan SCORE was 4.2 ± 2.8%.

The size of the prosthetic valve used is shown in Table II. Mechanical valves were used in 27 patients and bioprostheses were used in 13. A small prosthesis sized 19 mm or less was used in 34 out of 40 (85%) cases. The EOAI was 0.99 ± 0.15 cm$^2$/m$^2$ and PPM occurred in 8 patients, all being moderate with the EOAI ranging from 0.71 to 0.85 cm$^2$/m$^2$. Preoperative left ventricular ejection fraction was not different between the groups with and without PPM (62 ± 16% versus 59 ± 14%, $P = 0.64$).

Operative mortality occurred in 2 patients (5.0%), neither of whom had PPM. A 75-year-old female with chronic kidney disease died of nonocclusive mesenteric ischemia 14 days after surgery and a 91-year-old male died of deep sternal infection 24 days after surgery. Operative morbidity occurred in 6 cases: 3 with wound infection, 2 with prolonged ventilation, and 1 with new maintenance dialysis.

Follow-up of hospital survivors was 100% complete at a mean of 51.0 ± 30.8 months (range, 5–126 months). The actuarial survival was 92.5% at 1 year and 77.9% at 5 years (Figure 1). There was no significant difference in survival between cases with and without PPM ($P = 0.87$) (Figure 2). The overall freedom from a major cardiac or cerebrovascular event was...
97.4% at 1 year and 88.9% at 5 years (Figure 3). PG measured by echocardiography decreased from 82 ± 25 to 27 ± 14 mmHg ($P < 0.0001$) in the group without PPM, and from 113 ± 39 to 28 ± 13 mmHg ($P = 0.001$) in the group with PPM. LVMI decreased from 229 ± 80 to 161 ± 65 g/m$^2$ in the group without PPM ($P < 0.0001$), and from 216 ± 65 to 132 ± 24 g/m$^2$ ($P = 0.009$) in the group with PPM. Reduction of PG was significantly greater in the group with PPM than without PPM ($P = 0.02$) (Figure 4). Reduction of LVMI was not significantly different between the groups with and without PPM ($P = 0.58$) (Figure 5). NYHA functional class significantly improved in the entire cohort and the improvement was not significantly different between the groups with and without PPM ($P = 0.68$). One patient started using a cane to walk after surgery. All other survivors regained preoperative ADL after surgery.

**Discussion**

Recent progress in medical care has led to rapid aging of the population in many countries. In Japan, in 2010, the life expectancy at 75 years of age was reported to be an additional 11.58 years for males and 15.38 years for females. According to a recent study, AS due to age-related degeneration is becoming more common in the elderly. Severe AS requires AVR. When the aortic annulus of the patient is too small to allow a prosthetic valve with enough EOA in relation to the body surface area, the transvalvular gradient remains high, the prosthesis remains stenotic, and left ventricular hypertrophy does not regress, leading to negative outcomes. An EOA less than 0.85 cm$^2$/m$^2$ is generally regarded as the threshold for PPM, however, it is still controversial as to whether moderate PPM influences long-term survival, especially for the elderly. In
our series of patients aged 75 years or older, moderate PPM did not negatively influence long-term survival or regression of PG and LVMI. Negative outcomes following PPM are considered to be caused by higher PG, which is exemplified by the equation $\frac{P_g}{Q} = \frac{Q}{k \times EOA}$ in which $Q$ denotes transvalvular flow or cardiac output, and $k$ is a constant. Exercise stress physiologically increases cardiac output, but this response diminishes with age, although resting cardiac output does not vary significantly with age. This reduced response, together with decreased activities of daily life of the elderly, might result in regression of average cardiac output, contributing to the comparatively low PG of elderly patients with PPM.

The actual EOA is only measured in vivo after implantation of the prosthesis because it is influenced by a variety of factors including hemodynamics and the anatomical configuration of the left ventricular outflow tract, and the value varies depending on the hemodynamic circumstances. It is essential to obtain the estimated EOA of each particular prosthesis at surgery in order to decide whether to perform aortic root enlargement to avoid severe PPM. Preoperatively available values are practically more important for surgeons to map out the optimal surgical strategy. Therefore, the values of the effective prosthetic valve area provided by the manufacturer of the prosthesis, rather than postoperative echocardiographic data, were used to evaluate PPM in this study.

Even if moderate PPM is acceptable in the elderly, aortic root enlargement is desirable in certain situations. The preoperative left ventricular ejection fraction was fairly preserved in both groups with and without PPM in this study. This also might be why PPM did not influence the late survival and regression of PG and LVMI. The negative impact of PPM increases with the presence of impaired left ventricular function. Therefore, aortic root enlargement should be considered for patients with a poor ventricle in order to eliminate potential harmful consequences due to PPM. The risk of bleeding complications related to warfarin and other anticoagulant therapy increases with age. If the annulus of the patient who benefits from a bioprosthetic valve is too small for a 19-mm bioprosthesis, aortic root enlargement should be considered in order to implant a bioprosthesis. The body surface area of the patients was fairly small (average, 1.45 m²) in the current study. As a result, the patients with PPM all received only the next size down from the matched prosthesis and not any further down. If the annulus is too small to allow the next smaller size, again, aortic root enlargement should be considered to avoid severe PPM.

This review has certain limitations. It is a small population retrospective study including only 8 cases with PPM. The mean follow-up period was only 51 months and this might not have been long enough to show any significant differences. However, of particular note is that, in our series of patients 75 years of age or older, those with moderate PPM were not inferior in survival or reduction of PG and LVMI. Reduction of PG was even greater in the group with PPM. In addition, all survivors but one regained preoperative ADL after surgery.

In conclusion, AVR for elderly patients with AS was carried out safely with a risk similar to publicly-available predicted early mortality. Moderate PPM did not influence survival or reduction of PG or LVMI in these cases with significantly well preserved left ventricular function.

REFERENCES