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The long-term results and changing patterns of biological valves at the mitral position in contemporary practice in Japan

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ABSTRACT

Mitral valve surgery has changed with the wide acceptance of mitral valve repair. The aim of this study is to obtain the long-term results of patients who underwent mitral valve replacement (MVR) using a biological prosthesis in contemporary practice in Japan. From January 1990 to December 2013, 76 patients underwent MVR using a biological prosthesis with or without concomitant surgery. Data were obtained by means of a questionnaire and a telephone interview. The mean follow-up period was 4.26 years. The etiologies of the patients included dilated cardiomyopathy (DCM) (n=20 [26.3%]), ischemic mitral regurgitation (n=7 [9.2%]). There is a trend towards decreasing number of rheumatic and degenerative disease and increasing number of DCM and ischemic mitral regurgitation. Three patients (3.9%) died in the perioperative period. The 5- and 10-year overall survival rates were 69.6% and 31.7%, respectively. The 5- and 10-year freedom from valve related death were 95.6% and 80.6 %, respectively. The linearized rates of valve-related complications were as follows: thromboembolism (0.63%/patient/year), bleeding (1.25%/patient/year). One patient underwent reoperation for structural degeneration 13 years after the first operation. The present study shows the long-term results of mitral valve replacement with bioproshtesis in a contemporary case series. The practice pattern is changing. The low rate of valve-related complication justify the current patient selection.

Key Words: Imitral valve replacement; biological prosthesis; long-term results

INTRODUCTION

Mitral valve surgery has changed dramatically with the popularization of mitral valve repair. The superiority, in terms of clinical outcomes, of mitral valve repair over mitral valve replacement have made it the procedure of choice for the treatment of most pathological conditions of the mitral valve.[1)] Many papers which provided the long-term results of mitral valve replacement (MVR) using a biological prosthesis were from an era in which mitral valve repair was less popular.[2)] The patients who currently undergo MVR differ from the patients of the previous era

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of MVR.[3]

The aim of the present study is to investigate the long-term results of MVR with a biological mitral valve prosthesis in the current era of MVR surgery in Japan.

MATERIALS AND METHODS

From January 1990 to December 2013, 76 patients underwent MVR using a biological prosthesis with or without concomitant aortic valve surgery, tricuspid valve surgery, the MAZE procedure, or a coronary artery bypass in out institution. During the study period, 328 mechanical mitral valve replacements were performed.

The choice between a mechanical or biological prosthesis was made on an individual basis by surgeons and patients. Generally speaking, patients who were over 70 years of age with rheumatic disease and a degenerative etiology were indicated for MVR with a bioprosthesis rather than a mechanical valve. Biological valves were considered for younger patients when they had dilated cardiomyopathy, ischemic mitral regurgitation or if their life expectancy was short due to comorbidities. Biological valves were also considered for female patients of a very young age who wished to have children.

The data from all of the patients who underwent cardiac surgery at our institution after 1989 were prospectively entered into a computer database. In addition, questionnaires were mailed to all of the patients who had undergone valve surgery with the interval of three to five years. If the questionnaires were not returned, telephone or personal interviews were conducted.

Morbidity and mortality were defined according to the guidelines of The Society of Thoracic Surgeons and the American Association for Thoracic Surgery.[4] Standard operative techniques were employed for most cases with standard cardiopulmonary bypass and myocardial protection with blood cardioplegia. In some cases in which ventricular function was with severely depressed, mitral valve replacement was performed with a beating heart.

The bioprosthesis was implanted with pledgeted interrupted sutures. The posterior leaflet or both leaflets were preserved when possible. Coumadin was administered for three month; the anticoagulation treatment was discontinued and low dose aspirin was started if the patient showed normal sinus rhythm.

Categorical variables were expressed as numbers and percentages, while continuous variables were expressed as the mean ±SD. Early events were calculated as simple percentages. Linearized rates were calculated for late events (>30 days after surgery) representing the number of complications per 100 valve-years. Kaplan-Meier curves, including both early and late events, are presented. The testing of differences among the survival curves was performed using the log-rank test. For testing the differences among multiple groups were first assessed by an ANOVA followed by the Tukey–Kramer honestly significant difference test.

Seventy-six patients were included. The follow-up rate was 99%. The mean follow-up period was 4.26 years. The preoperative characteristics of the patients are listed in Table 1. The mean age at mitral valve replacement was 69.2 years. Forty-one patients were female. The etiologies varied and included a significant number of patients with functional mitral regurgitation. Twenty patients (26.3%) had dilated cardiomyopathy (DCM) and 7 patients (9.2%) had ischemic mitral regurgitation. There were 27 patients (35.5%) with rheumatic disease, and 12 patients (15.8%) with degenerative disease. Six patients (7.9%) underwent MVR for infective endocarditis. Three patients underwent reoperation for structural degeneration of the previous bioprosthesis, 2 of whom underwent surgery at other hospitals. One patient underwent MVR for papillary muscle rupture after acute myocardial infarction.

Table 1 Pre-operative variables

Mitral prostheses (n)	76
Patients (n)	76
Age (y) Mean(SD)	69.2 (11.6)
Gender	
Male	35
Female	41
Etiology	
Degenerative	12 (15.8%)
SVD	3 (4.0%)
Rheumatic	27 (35.5%)
Endocarditis	6 (7.9%)
DCM	20 (26.3%)
Ischemic	7 (9.2%)
Papillary muscle rupture	1 (1.3%)
Preoperative NYHA	
I	13 (17.1%)
II	19 (25.0%)
III	26 (34.2%)
IV	18 (23.7%)
Preoperative LVEF (%)	
≧50	43 (56.6%)
36–50	13 (17.1%)
≦35	20 (26.3%)

SD, Standard Deviation; SVD, Structural Valve Degeneration of Bioprosthesis; DCM, Dilated Cardiomyopathy; ICM, ; NYHA, NewYork Heart Association Class; LVEF, Left Ventricular Ejection Fraction

There is a trend towards decreasing rate of rheumatic and degenerative disease and increasing number of DCM and ischemic mitral regurgitation (Figure 1). Total number of mitral valve surgery as well as other open heart surgery is increasing in our institution.

The operative variables are listed in Table 2. All patients underwent mitral valve replacement with either bovine or porcine stented valves. Forty-three patients (59.2%) underwent concomitant tricuspid valve surgery. Twenty-three patients (30.3%) underwent a concomitant MAZE procedure.

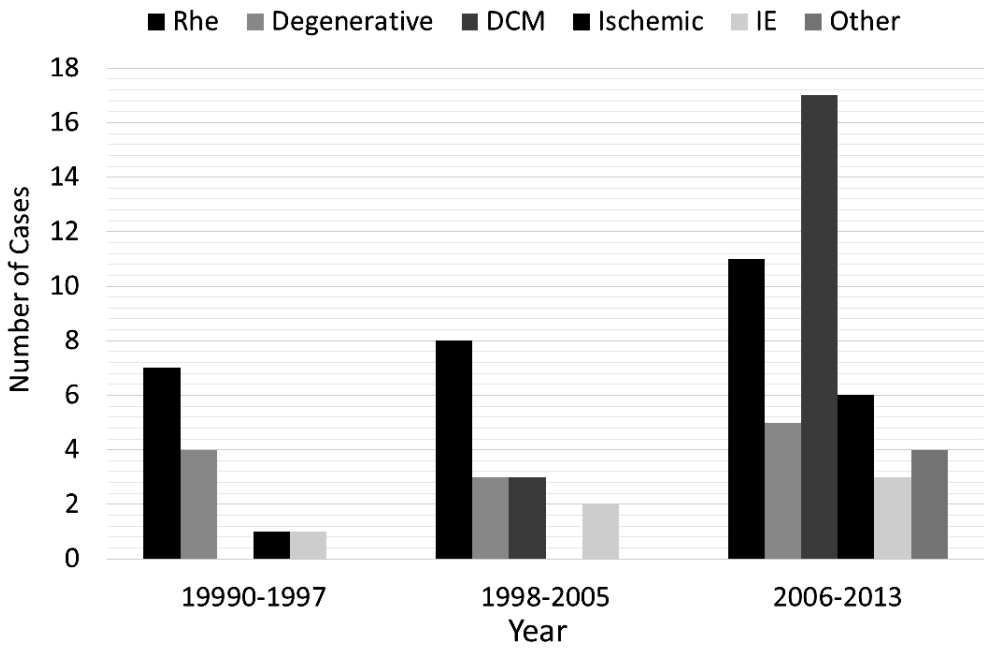

Fig. 1 Percentages o each etiology of mitral valve disease for three periods. The numbers in the bars indicate actual number of cases.
Rhe, Rheumatic Disease; DCM, Dilated Cardiomyopathy; Ischemic, Ischemic Mitral Regurgitation; IE, Infective Endocarditis

Table 2 Operative variables

Mitral Prosthesis	
CEP	25 (32.9%)
Mosaic	23 (30.2%)
CESAV	1 1(14.5%)
Epic	17 (22.4%)

Concomitant Surgery	
AVR	17 (22.4%)
TVR	2 (2.5%)
TAP	43 (59.2%)
MAZE	23 (30.3%)
CABG	5 (6.6%)

Re-sternotomy	5 (6.6%)
Emergency Surgery	4 (5.3%)
Surgery done on beating heart	4 (5.3%)

Prosthesis Size	
25	12 (15.8%)
27	39 (51.3%)
29	20 (26.3%)
31	5 (6.6%)

CEP, Carpentier Edwards Pericardial Valve; CESAV, Carpentier Edwards Supraanular Porcine Valve, AVR, Aortic Valve Replacement; TVR, Tricuspid Valve Replacement; TAP, Tricuspid Annuloplasty; CABG, Coronary Artery Bypass Grafting

RESULTS

Operative Mortality, Functional Status, and Survival Rates

Three patients died in the perioperative period for a total in-hospital mortality rate of 3.9%. A total of 25 late deaths were recorded, for a linearized rate of 1.56%/valve-year (Figure 2). Of these, 5 deaths were considered to be valve-related (hemorrhage [n=1], endocarditis [n=1], and sudden death [n=3]). The overall 5- and 10-year survival rates were 69.6 % and 31.7%, respectively (Figure 2A). The 5- and 10-year freedom from valve-related death were 95.6% and 80.6%, respectively (Figure 2B).

Valve-Related Complications

No cases of valve thrombosis were reported. A total of 2 thromboembolic events were reported for a linearized rate of 0.63 %/patient/year. The 5- and 10-year freedom from thromboembolism rates were 96.6% and 87.8%, respectively.

A total of 4 bleeding events were reported for a linearized rate of 1.25%/valve-year. One patient died as a result of a bleeding event. The 5- and 10-year freedom from bleeding events rates were 90.7% and 75.5%, respectively.

Endocarditis was reported in 3 patients; none of whom underwent reoperation. One patient died without reoperation. The linearized rate was 0.94%/patient/year.

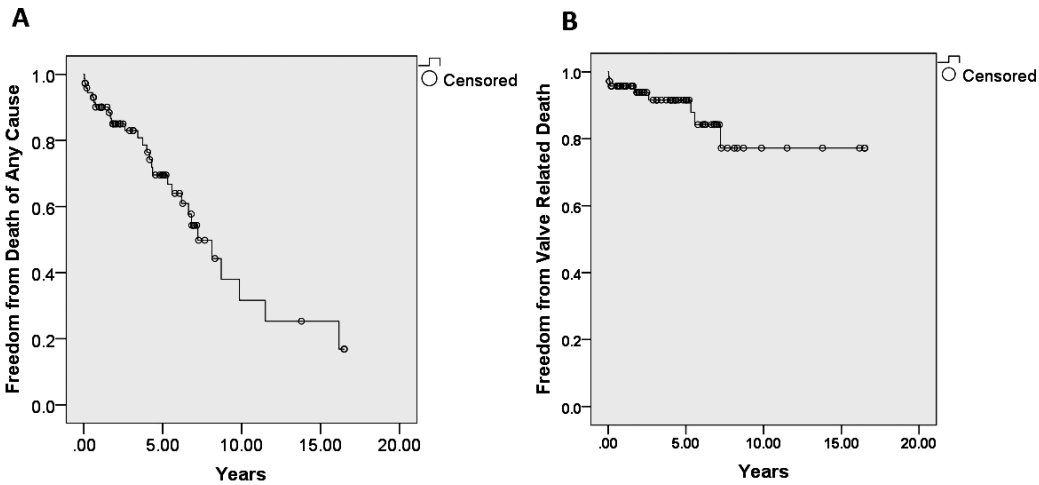

Fig. 2 **A**, Freedom from death of any cause; **B**, Freedom from Valve Related Death

Table 3 patient demographics for each pathologies

	Rheumatic (27)	Degenerative (12)	IE (6)	DCM (20)	Ischemic (7)	SVD	ANOVA p
Age	70.4 (9.4)	71.3 (15.8)	62.0 (20.0)	66.2 (11.0)	71.4 (4.3)	58.3 (22.8)	n.s.
F/M	17/10	6/6	1/5	13/7	1/6	3/0	
Preop. NYHA	2.2	2.5	3.0	2.85	3.4	2.7	n.s.
LVEF	61.1 (13.4)[a,b]	64.4 (16.1)[c,d]	62.0 (20.0)	34.9 (11.0)[a,c]	36.2 (18.0)[b,d]	67.9 (11.8)	<0.001

a, b, c, d $p<0.05$ by Tukey–Kramer honestly significant difference test
DCM, Dilated Cardiomyopathy; IE, Infective Endocarditis; SVD, Structural Degeneration; PMR Papillary Muscle Rupture; ANOVA. Analysis of Variance; NYHA, New York Heart Association Class; LVEF, Left Ventricular Ejection Fraction

No nonstructural dysfunction occurred. No clinically significant hemolysis was recorded in the absence of structural valve dysfunction.

Structural valve deterioration occurred in one patient who had undergone mitral valve replacement at the age of 23. She underwent reoperation for structural degeneration 13 years after the initial operation.

We finally subdivided the cohort based on the etiology of the mitral valve disease. The characteristics of the patients with each etiology are shown in Table 3. The average date of surgery differed significantly among the different etiologies. In recent years, there have tended to be more patients with DCM and ischemic mitral regurgitation. In the earlier years of the study period, the rate of rheumatic valve disease was higher. There was a statistically significant difference in the average operation date in the patients with DCM and rheumatic disease. The average age of patients was youngest in the DCM group; however, the difference did not reach statistical significance in the ANOVA. There was a statistically significant difference in the left ventricular ejection fraction. There were statistically significant differences between the following groups: degenerative and ischemic, degenerative and DCM, rheumatic and DCM, and rheumatic and ischemic. The overall survival rates for all etiologies are shown in Figure 3.

In the final questionnaire, we found that 64.5% of the patients were taking Coumadin.

DISCUSSION

The present study shows the results of a contemporary series of patients who underwent MVR with a biological prosthesis in Japan in the current surgical era. With the wide acceptance of mitral valve repair, the indication for mitral valve replacement is limited, in most pathologies, to cases in which mitral valve repair is not technically feasible.[5] We also use mitral valve replacement in patients with functional MR that is associated with either dilated cardiomyopathy or ischemic cardiomyopathy when we are of the opinion that the potential survival offered by mitral valve replacement is equivalent or superior to that of repair.[6] Our results showed that only 15% of the patients had a degenerative pathology, which was the major underlying pathology of patients who had underwent mitral valve replacement in the previous era. That 35.5% of the patients in our present study were indicated due to rheumatic disease, and the rate is decreasing in recent years. The rate of patients with DCM (26.3%) and ischemic mitral regurgitation (9.2%) reflects the increasing application of these relatively new indications for mitral valve surgery.

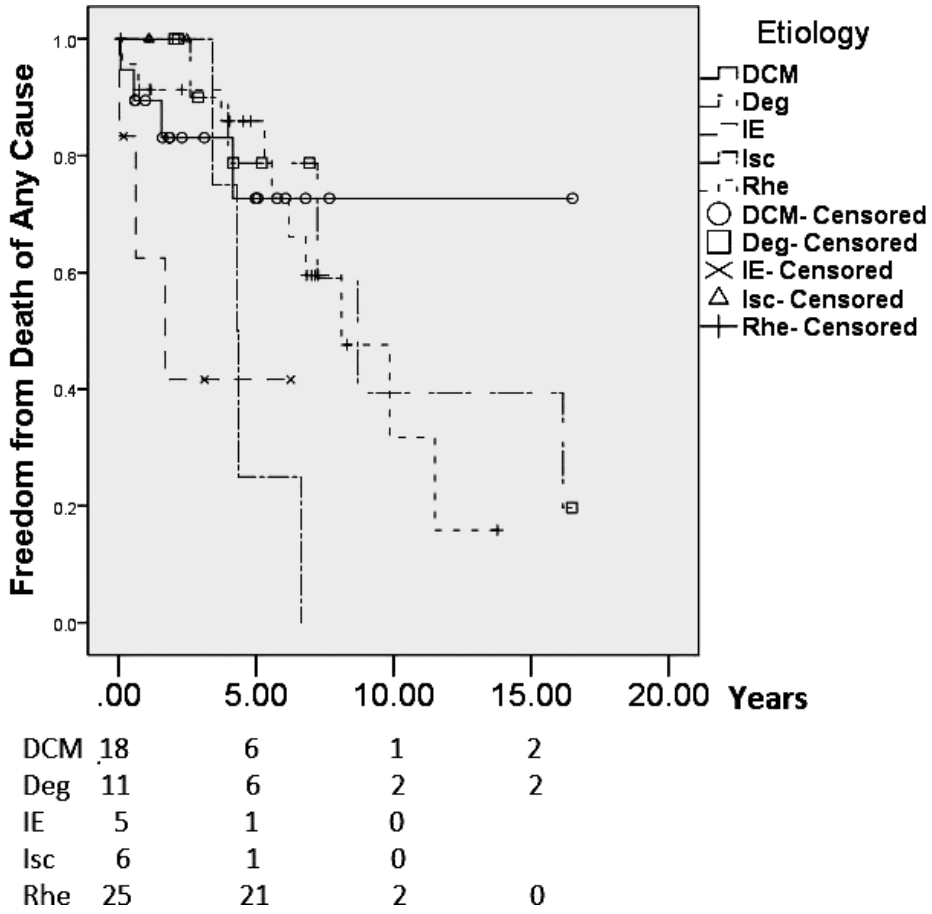

Fig. 3 Freedom from death of any cause for each etiology
DCM, Dilated Cardiomyopathy; Deg, Degenerative; IE, Infective Endocarditis; Isc, Ischemic Mitral Regurgitation SVD, Rhe, Rheumatic Disease

The cases of morbidity and mortality associated with the operated valves were greatly influenced by non-cardiac and non-valve-related cardiac mortality. Our results show the incidence of each valve-related complication in current practice in Japan.

Long-term survival was limited in the present study. Limited long-term survival has also been reported in other series.[7, 8] The mean age at mitral valve replacement was 69.2 years in our series. The limited overall survival is largely explained by the high average age at mitral valve replacement. Furthermore, suboptimal survival has also been reported in many studies on mitral valve surgery in patients with ischemic mitral regurgitation and dilated cardiomyopathy.

The linearized bleeding rate was 1.25% in our study. This is compatible with the rates reported in other studies. Bourguignon *et al.* reported a rate of 0.8%/patient/year, while Jamieson *et al.* reported a rate of 0.91%/patient/year. The linearized rate of thromboembolism was 0.63/patient/year in the present study. This is also compatible with previous reports. Bourguignon *et al.* reported a rate of 0.7%/patient/year, while Jamieson *et al.* reported a rate of 3.19%/patient/year. We noted that 64.5% of our patients were taking Coumadin in our cross-sectional survey. This is much higher than the rates reported in previous studies. In the cohort of one randomized

controlled study, 15% of the patients with a mitral prosthesis were receiving Coumadin at five years; this proportion rose to 57% in later years. This may explain why the relatively high bleeding rate and relatively low thromboembolism rate in the patients of the present study.

There was only one case of valve explant due to SVD in the present study. The explant occurred in a very young patient at 13 years after the initial MVR. Since SVD is the most important drawback of biological valves, it could be said that that valve choice seems to be appropriate in our patient population. However, we found that a significant percentage of the patients in the present study were taking Coumadin despite the use of a bioprosthesis. Since randomized controlled trials have demonstrated that the lower rate of bleeding complications is the only benefit of bioprosthesis, this may raise a question as to how much of a benefit the choice of a biological prosthesis offers over a mechanical prosthesis.

CONCLUSIONS

The present study shows the long-term results of mitral valve replacement in a contemporary series. The practice pattern of mitral valve replacement with biological prosthesis in Japan is changing in terms of etiology of mitral valve disease. The low rate of valve-related complications and small number of explants due to SVD justify the current practices.

DISCLOSURES

The authors have no conflict of interest to disclose.

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