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Surgical Treatment of Degenerative Mitral Valve Regurgitation in the Elderly: Comparison of Early and Long-Term Outcomes Using Propensity Score Matching Analysis

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Background: It is unclear whether mitral valve (MV) repair for degenerative mitral regurgitation (MR) provides the same advantages in the elderly that it does in the general population. **Methods:** From 1994 to 2016, 188 elderly patients (mean age, 68.3±5.50 years) underwent MV repair (n=153) or MV replacement (n=35) for primary degenerative MR. Early and long-term outcomes were compared before and after propensity score matching (PSM). **Results:** Before PSM, there was a significant difference in operative mortality (p=0.011). Overall survival and freedom from cardiac-related death (CRD) at 5, 10, and 15 years were significantly higher in patients who underwent MV repair (p=0.039 and p=0.007, respectively). In the multivariable analysis, MV replacement was an independent risk factor of CRD. After PSM, operative mortality was not significantly lower in patients who underwent MV repair (p=0.125). Overall survival and freedom from CRD at 5, 10, and 15 years showed no significant difference between the 2 groups in the PSM cohort (p=0.207, p=0.47, respectively). There was no significant difference in freedom from reoperation before or after PSM (p=0.963 and p=0.575, respectively). **Conclusion:** MV repair for primary degenerative MR might be a valid option in the elderly population if successful repair is possible.

Key words: 1. Mitral valve insufficiency
2. Mitral valve annuloplsty
3. Heart valve prosthesis implantation
4. Aged

Introduction

Current European and American guidelines recommend mitral valve (MV) repair as the treatment of choice for primary degenerative mitral regurgitation (MR) in the general population [1,2]. However, controversy exists regarding whether MV repair provides the same advantages as MV replacement in terms of operative mortality, long-term survival, and valve-related complications in the elderly population [3-10]. The aim of this study was to compare the early and long-term clinical outcomes of MV repair and MV replacement in elderly patients.

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Table 1. Preoperative demographic and echocardiographic data

Characteristic	All study patients			Matched groups		
	MV repair (n=153)	MV replacement (n=35)	p-value	MV repair (n=31)	MV replacement (n=31)	p-value
Age (yr)	68.1±5.52	69.1±5.43	0.324	68.2±5.92	68.8±5.40	0.630
Male	75 (49.0)	18 (51.4)	0.797	16 (51.6)	15 (48.3)	>0.999
Body mass index ≥25.0 kg/m^2	51 (33.3)	11 (31.4)	0.829	11 (35.4)	11 (35.4)	>0.999
New York Heart Association class ≥3	66 (43.1)	28 (80.0)	<0.001	25 (80.6)	24 (77.4)	>0.999
Risk factors						
Smoking	22 (14.4)	4 (11.4)	0.790	3 (19.3)	4 (12.9)	>0.999
Diabetes mellitus	26 (17.0)	8 (22.9)	0.416	4 (12.9)	6 (19.3)	0.754
Hypertension	68 (44.4)	15 (42.9)	0.865	15 (48.3)	14 (45.1)	>0.999
Stroke	9 (5.90)	4 (11.4)	0.267	2 (6.45)	3 (19.3)	>0.999
Dyslipidemia	11 (7.2)	1 (2.9)	0.700	1 (3.22)	1 (3.22)	>0.999
Chronic obstructive pulmonary disease	3 (2.00)	2 (5.70)	0.233	1 (3.22)	1 (3.22)	>0.999
Chronic kidney disease	24 (15.7)	8 (22.9)	0.309	8 (25.8)	7 (22.5)	>0.999
Coronary disease	22 (14.4)	5 (14.3)	0.989	3 (19.3)	3 (19.3)	>0.999
Peripheral vascular disease	7 (4.60)	1 (2.90)	>0.999	1 (3.22)	1 (3.22)	>0.999
Atrial fibrillation	69 (45.1)	21 (60.0)	0.111	15 (48.3)	17 (54.8)	0.804
Emergency	2 (1.30)	2 (5.70)	0.158	1 (3.22)	0	>0.999
Euro-SCORE II	2.56±1.59	3.60±2.24	0.010	2.82±1.61	3.55±2.32	0.165
Echocardiography						
Left ventricle ejection fraction (%)	60.4±8.36	56.9±10.1	0.039	58.3±10.1	58.4±8.64	0.969
Left ventricle end-systolic dimension (mm)	38.6±7.67	40.0±9.56	0.372	40.2±7.87	39.2±7.57	0.592
Tricuspid regurgitation ≥moderate	29 (19.0)	9 (25.7)	0.369	8 (25.8)	7 (22.5)	>0.999

Values are presented as mean±standard deviation or number (%).
MV, mitral valve.

Methods

1) Patient characteristics

The study protocol was reviewed by the Institutional Review Board of Seoul National University Hospital and approved as a minimal-risk retrospective study (IRB approval no., H-1801-033-913) that did not require personal agreement based on our institutional guidelines. From January 1994 to December 2016, 188 patients who were older than 60 years (mean, 68.3±5.50 years; 93 males and 95 females) underwent MV repair (n=153, 82.3%) or MV replacement (n=35, 17.7%) for primary degenerative MR at Seoul National University Hospital. Cases of degenerative MR combined with other etiologies, such as rheumatic disease, congenital conditions, ischemia, and infection, were excluded. Six patients in whom MV repair was attempted, but was changed to MV replacement, were included in the MV repair group, as we utilized an intention-to-treat analysis. To overcome the baseline differences between the 2 groups, propensity score matching analysis was performed in a 1:1 manner with 25 common variables, and 31 patients were extracted from each group. Before matching, patients who underwent MV repair were less likely to be New York Heart Association (NYHA) functional class III/IV ($p<0.001$) and were more likely to have a good left ventricular (LV) ejection fraction (p=0.039) and Euro-SCORE II (p=0.01). However, after propensity score matching, there were no significant differences in the preoperative demographic and echocardiographic data between the 2 groups (Table 1).

2) Surgical procedures and operative data

All procedures were performed through median sternotomy and aorto-bicaval cannulation under moderate hypothermia and antegrade cold cardioplegic arrest. Primary degenerative MR was defined as leaflet prolapse due to chordal elongation or rupture, and the preoperative echocardiographic findings were confirmed through direct surgical inspection with

Table 2. Operative data

Variable	All study patients			Matched groups		
	MV repair (n=153)	MV replacement (n=35)	p-value	MV repair (n=31)	MV replacement (n=31)	p-value
Cardiopulmonary bypass time (min)	198±75.4	203±79.8	0.733	211±69.1	210±81.4	0.965
Aortic cross-clamp time (min)	127±48.4	128±60.8	0.927	138±47.2	135±60.1	0.856
Concomitant procedures						
Aortic valve	15 (9.80)	6 (17.1)	0.235	3 (19.3)	5 (16.1)	0.687
Tricuspid valve	42 (27.5)	12 (34.3)	0.420	12 (38.7)	11 (35.4)	>0.999
Coronary artery bypass graft	11 (7.20)	1 (2.90)	0.700	2 (6.45)	1 (3.22)	>0.999
Arrhythmia	46 (30.1)	11 (31.4)	0.874	9 (29.0)	11 (35.4)	0.791
Aorta procedure	8 (5.20)	2 (5.70)	>0.999	1 (3.22)	2 (6.45)	>0.999

Values are presented as mean±standard deviation or number (%).
MV, mitral valve.

pathologic results showing fibromyxoid degeneration. Four surgeons participated in this study and 2 specialized valve surgeons performed 162 cases (86.1%). The decision of whether to perform MV repair or MV replacement was determined by the operating surgeon, but MV repair is generally the preferred method at our institution. Various repair techniques for the valve itself were used based on the surgeon's preference, including leaflet resection and annular plication, neo-chordal formation, chordal shortening, and chordal transfer, while most of the cases were accompanied with annuloplasty (n=130, 88.4%). The subvalvular apparatus–sparing technique was performed in patients who underwent MV replacement whenever possible, and a tissue valve was implanted in most cases (n=36, 87.5%). The mean cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times were 199±76.5 minutes and 127±50.9 minutes, respectively. Concomitant procedures were performed, including aortic valve procedures (n=21), tricuspid valve procedures (n=54), coronary artery bypass surgery (n=12), arrhythmia surgery (n=57), and ascending aorta replacement (n=10). There were no statistically significant differences between the 2 groups in the operative data before or after propensity score matching (Table 2).

3) Antithrombotic and antiplatelet management

Anticoagulation (warfarin sodium) was adjusted to obtain a target international normalized ratio of 2.0 to 2.5 for 3–6 months in most of the patients who underwent MV repair and bioprosthetic MV replacement. Lifelong anticoagulation was maintained in patients who underwent mechanical MV replacement or who had persistent atrial fibrillation after MV repair or replacement. A specialized anticoagulation service team, composed of experienced pharmacists, regularly followed up all patients who were prescribed oral anticoagulants.

4) Evaluation of early and long-term clinical outcomes

Patients underwent regular postoperative follow-up at the outpatient clinic at 3- or 4-month intervals. Data about vital status and cardiac-related death were obtained via Statistics Korea and were complete for all patients. Clinical follow-up was closed on December 30, 2017, with a median follow-up duration of 206.3 months (range, 1–280 months) in the MV repair group and 143.1 months (range, 1–226 months) in the MV replacement group. Operative mortality was defined as any death within 30 days after surgery or during the same hospital admission. Low cardiac output syndrome (LCOS) was diagnosed if patients needed mechanical or continuous inotropic infusion to maintain systolic blood pressure. Postoperative respiratory complications included pneumonia or prolonged ventilator care for more than 72 hours. Chronic kidney disease (CKD) and acute kidney injury were defined as a glomerular filtration rate <60 mL/min/1.73 m^2 and an increase of $>50\%$ in serum creatinine level from the preoperative value, respectively. Mitral valve-related events (MVREs) included those identified in previous guidelines [11]: (1) cardiac death; (2) structural valve deterioration (SVD) and nonstructural valve dysfunction (NSVD);

Table 3. Comparison of early clinical outcomes

Variable	All study patients			Matched groups		
	MV repair (n=153)	MV replacement (n=35)	p-value	MV repair (n=31)	MV replacement (n=31)	p-value
Operative mortality	6 (3.90)	6 (17.1)	0.011	1 (3.20)	5 (16.1)	0.125
Complications						
Low cardiac output syndrome	19 (12.4)	12 (34.3)	0.002	6 (19.3)	9 (29.0)	0.581
Bleeding	9 (5.9)	1 (2.90)	0.691	3 (9.67)	0	0.250
Acute kidney injury	12 (7.80)	6 (17.1)	0.111	3 (9.67)	5 (16.1)	0.625
Arrhythmia	42 (27.5)	7 (20.0)	0.365	9 (29.0)	6 (19.3)	0.549
Mediastinitis	5 (3.30)	0	0.586	3 (9.67)	0	0.250
Cerebrovascular accident	5 (3.3)	3 (8.6)	0.169	1 (3.20)	3 (9.67)	0.500
Respiratory	32 (20.9)	11 (31.4)	0.182	6 (19.3)	9 (29.0)	0.549

Values are presented as number (%).
MV, mitral valve.

(3) MV reoperations; (4) composite thrombosis, embolism, bleeding (CTEB) events that caused hospitalization, permanent injury, or death; and (5) congestive heart failure requiring readmission.

5) Statistical analysis

Statistical analysis was performed using IBM SPSS ver. 23.0 (IBM Corp., Armonk, NY, USA). Data were expressed as mean±standard deviation, median with ranges, or proportions. Comparisons between the 2 groups were performed with the chi-square or Fisher exact tests for categorical variables and the Student t-test for continuous variables. To adjust for baseline differences and selection bias between the 2 groups, propensity score matching was performed with a logistic regression analysis. The underlying variables used to estimate the propensity score included the following: age, sex, body mass index $\geq$25 kg/m^2, NYHA functional class$\geq$3, smoking, diabetes mellitus, hypertension, history of stroke, dyslipidemia, chronic obstructive pulmonary disease, CKD, coronary artery disease, peripheral vascular disease, atrial fibrillation, emergency operation, LV ejection fraction, LV end-systolic dimension, tricuspid regurgitation $\geq$moderate, CPB time, ACC time, aortic valve procedure, tricuspid valve procedure, coronary artery bypass surgery, arrhythmia surgery, and ascending aorta replacement. The McNemar test and the paired Student t-test were calculated to compare the categorical and continuous variables between the matched groups. Survival rates were estimated using the Kaplan-Meier method, and between-group comparisons were performed using the log-rank test. The Cox proportional hazard model was adopted for analyses of risk factors for time-related events. All p-values less than 0.05 were considered to indicate statistical significance.

Results

1) Early outcomes

Operative mortality occurred in 12 patients (MV repair, 6 of 153 patients [3.9%]; MV replacement, 6 of 35 patients [17.1%]; p=0.011). Early postoperative morbidities included LCOS (n=31, 16.5%), postoperative bleeding requiring reoperation (n=10, 5.3%), acute kidney injury (n=18, 9.6%), arrhythmia (n=49, 26.1%), mediastinitis (n=5, 2.7%), stroke (n=8, 4.3%), and respiratory complications (n=43, 22.9%). The incidence of LCOS was significantly higher in the MV replacement group than in the MV repair group (MV repair, n=19 [12.4%]; MV replacement, n=12 [34.3%]; p=0.002). However, after propensity score matching, there were no significant differences in operative mortality (MV repair, n=1 [3.20%]; MV replacement, n=5 [16.1%]; p=0.125) or early postoperative morbidity between the 2 groups (Table 3).

2) Long-term outcomes

Among the 176 early survivors, late death occurred in 44 patients, including 13 cardiac deaths. Overall survival at 5, 10, and 15 years was 83.5%, 70.9%, and 57.7% in patients who underwent MV repair versus 74.3%, 52.5%, and 42.0% in those who under-

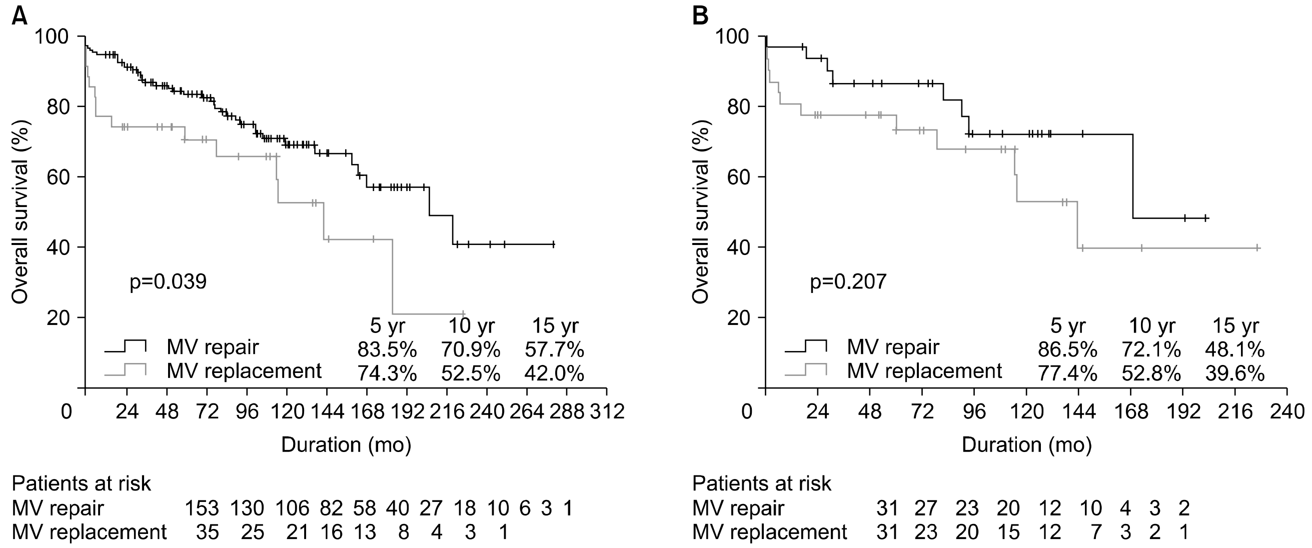

Fig. 1. Comparison of overall survival in the MV repair and MV replacement groups (A) before and (B) after propensity score matching. MV, mitral valve.

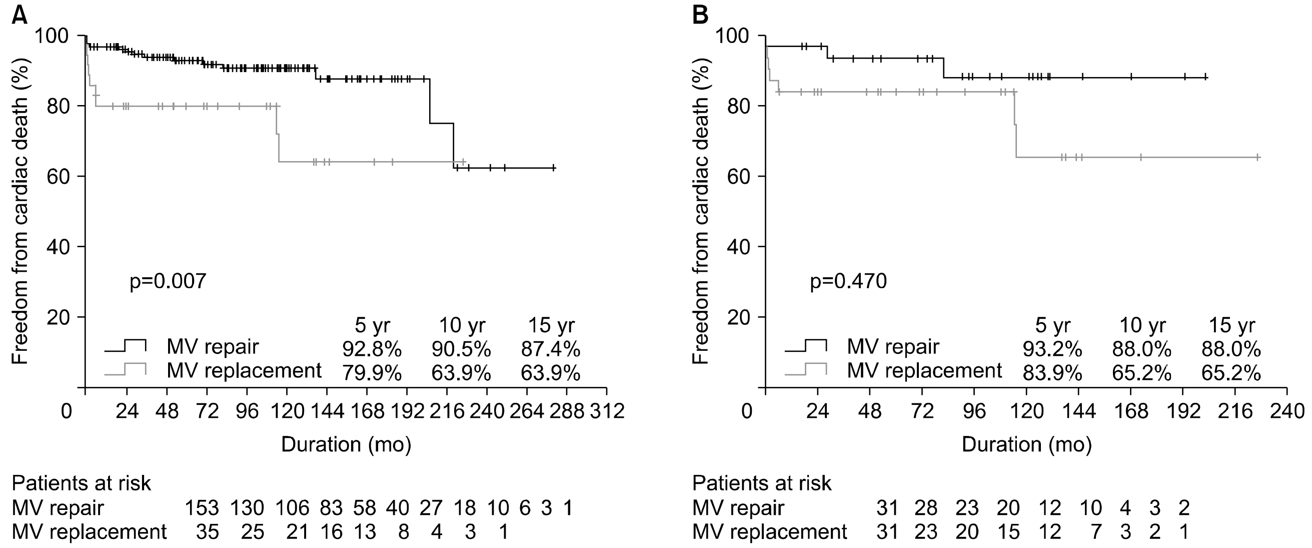

Fig. 2. Comparison of freedom from cardiac-related death in the MV repair and MV replacement groups (A) before and (B) after propensity score matching. MV, mitral valve.

went MV replacement, respectively (p=0.039) (Fig. 1A). The rate of freedom from cardiac death at 5, 10, and 15 years was 92.8%, 90.5%, and 87.4% in the MV repair group versus 79.9%, 63.9%, and 63.9% in the MV replacement group, respectively (p=0.007) (Fig. 2A). After propensity score matching, the 5-, 10-, and 15-year overall survival rate (86.5%, 72.1%, and 48.1% in the MV repair group versus 77.4%, 52.8%, and 39.6% in the MV replacement group, respectively; p=0.207) (Fig. 1B) and the rate of freedom from cardiac-related death (93.2%, 88.0%, and 88.0% in the MV repair group versus 83.9, 65.2%, and 65.2% in the MV replacement group, respectively; p=0.470) (Fig. 2B) were still higher in the MV repair group, although there were no statistically significant differences between the 2 groups. Cox proportional hazard analysis was performed on cardiac-related death in the overall cohort and demonstrated that MV replacement and CKD were independent risk factors for cardiac-related death (Table 4).

Table 4. Univariate and multivariable risk factor analysis for cardiac-related death in the overall cohort

Variable	Univariate analysis	Multivariable analysis	
	p-value	Hazard ratio (95% confidence interval)	p-value
Mitral valve replacement	0.010	2.768 (1.107-6.921)	0.029
New York Heart Association class ≥3	0.075	1.310 (0.506-3.389)	0.578
Chronic kidney disease	0.001	3.095 (1.188-8.061)	0.021
Coronary disease	0.044	1.329 (0.330-5.356)	0.690
Cardiopulmonary bypass time (min)	0.007	1.004 (0.999-1.009)	0.142
Aortic cross-clamp time (min)	0.253	-	-
Combined coronary artery bypass graft	0.006	3.260 (0.680-15.626)	0.139
Operator	0.891	-	-

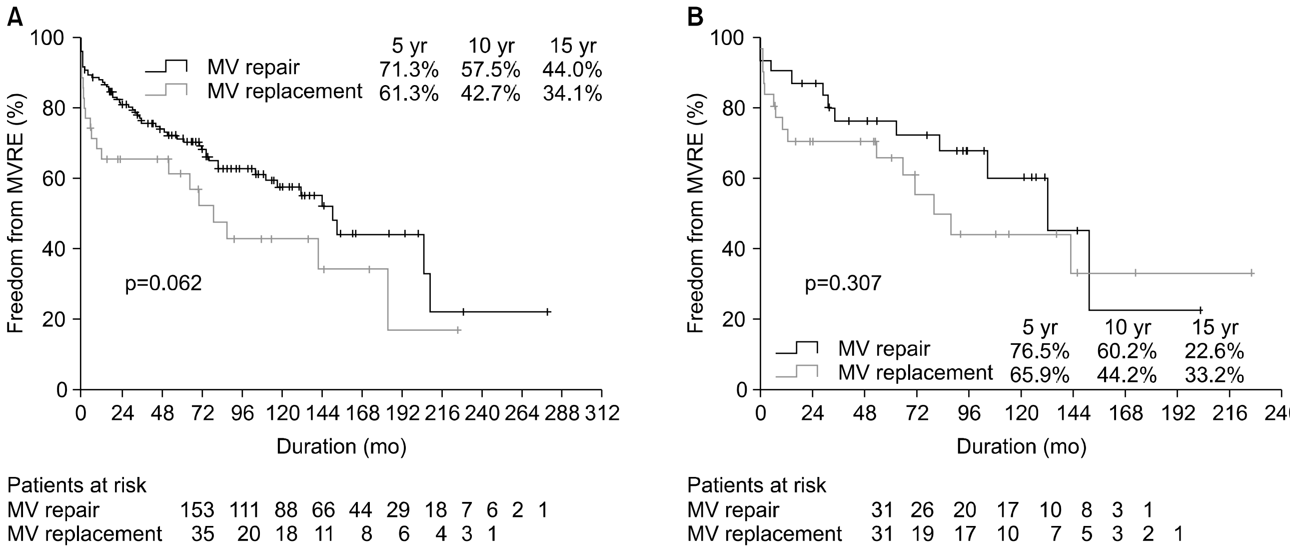

Fig. 3. Comparison of freedom from MVREs in the MV repair and MV replacement groups (A) before and (B) after propensity score matching. MV, mitral valve; MVRE, mitral valve-related event.

3) Mitral valve-related events

One or more MVRE occurred in 73 patients, including 13 reoperations. In the MV repair group, there were 25 and 1 patients who experienced SVD (MR ≥3+) and NSVD, respectively, and reoperations were performed in 11 patients. All these patients underwent MV replacement due to SVD (n=10) and hemolytic anemia (n=1). Oral anticoagulation was maintained for more than 6 months in 50 patients, and CTEB occurred in 16 patients (valve thrombosis [n=1]; embolism [n=9]; bleeding [n=10]). Readmission was required because of congestive heart failure in 25 patients. In the MV replacement group, SVD (MR ≥3+) and NSVD occurred in 1 and 2 patients. Redo MV replacement was performed in 2 patients due to SVD and pannus formation, respectively. An oral anticoagulant was maintained in 17 patients, and CTEB occurred in 8 patients (valve thrombosis [n=1]; embolism [n=2]; bleeding [n=8]). Readmission because of congestive heart failure was required in 7 patients. The 5-, 10- and 15-year rates of freedom from MVRE were 71.3%, 57.5%, and 44.0% in the MV repair group versus 61.3%, 42.7%, and 34.1% in the MV replacement group (p=0.062) (Fig. 3A). After propensity score matching, patients who underwent MV repair had a still higher tendency for freedom from MVREs at 5, 10, and 15 years (76.5%, 60.2%, and 22.6% in the MV repair group versus 65.9%, 44.2%, and 33.2% in the MV replacement group), although there were no significant differences between the 2 groups (p=0.307) (Fig. 3B). Among the MVREs, freedom from reoperation at 5, 10, and 15 years

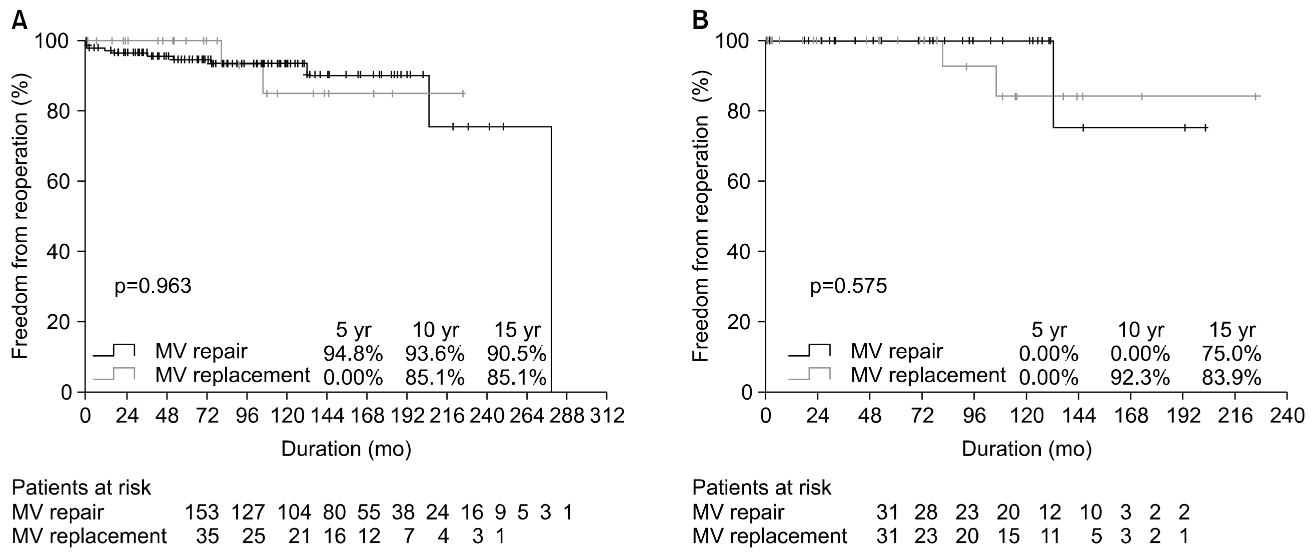

Fig. 4. Comparison of freedom from reoperations in the MV repair and MV replacement groups (A) before and (B) after propensity score matching. MV, mitral valve.

showed no significant differences before or after propensity matching (p=0.963 and p=0.575, respectively) (Fig. 4A, B).

Discussion

This study demonstrated that MV repair for primary degenerative MR might be a valid option in the elderly population if successful repair is possible. Overall survival and freedom from cardiac death showed more favorable trends in the MV repair group even after propensity score matching. MV replacement was an independent risk factor for cardiac-related death in the multivariable analysis.

Current European and American guidelines strongly recommend MV repair as the preferred surgical method, especially for degenerative mitral disease, in the general population [1,2]. MV repair has been associated with lower operative mortality, better long-term survival, and fewer valve-related complications than MV replacement [12]. However, the feasibility and efficacy of MV repair in the elderly population is still debated. Although some retrospective observational studies and meta-analyses have suggested that MV repair might have favorable results in early and long-term outcomes even in the elderly population [3-10], data obtained from administrative American databases showed a low rate of MV repair (<50%) in those older than 65 years [13,14]. Some operators, especially young surgeons, still considered older patients to be poor surgical candidates for MV repair for multiple reasons: (1) MV repair requires longer CPB and ischemic times, which can affect early and long-term clinical outcomes; (2) elderly patients tend to have a more friable or calcified leaflet and annulus, making repair technically more difficult, increasing the possibility of failure and reoperation; and (3) the shorter life expectancy of elderly patients may decrease the benefit of MV repair over MV replacement [5,8,9,15].

One of the most important considerations when comparing MV repair and MV replacement in the elderly population is that there might be baseline differences between the 2 groups. The patients who underwent MV repair had lower Euro-SCORE II (p=0.01), causing selection bias when comparing early and long-term clinical outcomes. To minimize this limitation, we only enrolled patients with primary degenerative MR who were older than 60 and performed propensity score matching using 25 variables. After propensity score matching, the preoperative demographic data were similar between the 2 groups. Despite the concerns that have been raised in this regard, CPB and ACC times were not significantly longer in the MV repair group before or after propensity score matching, which is similar to previous studies [3-6]. The CPB and ACC times (199±76.5 minutes and 127±50.9 minutes, respectively) were markedly longer than those reported in previous studies [3-8]. There are several reasons for this. First, this study included 19 patients who underwent MV surgery prior to the 2000s. Second, concomitant procedures such as aortic valve (n=21) and ascending aorta procedures (n=10), and redo surgery patients (n=3) who previously underwent cardiac procedures other than MV surgery, were included in the overall cohort [3,4]. Finally, 7 of 159 patients (5.3%) underwent MV repair but were converted to MV replacement, which is a slightly higher rate than reported in previous studies. Silaschi et al. [4] and Gaur et al. [5] reported that 4 of 224 patients (1.78%) and 10 of 566 patients (1.75%) experienced MV repair failure, respectively. CPB and ACC times were not found to be independent predictors affecting cardiac-related death in the multivariate analysis.

In our study, MV repair showed better early and long-term clinical outcomes than MV replacement. Before propensity score matching, operative mortality occurred in 12 patients (MV repair, 6 of 153 patients [3.9%]; MV replacement, 6 of 35 patients [17.1%]; p=0.011), and 11 cases experienced LCOS and cardiac-related death. The rates of overall survival and freedom from cardiac-related death were significantly higher in the MV repair group. The reduction of the rates of overall survival and freedom from cardiac-related death in the MV replacement group were mainly observed within 2 years after surgery. Enriquez-Sarano et al. [16] explained similar results by pointing out that the postoperative LV ejection fraction was significantly lower after MV replacement due to the change in the LV geometry, resulting in LCOS and cardiac-related death, thereby affecting overall survival. Similarly to our study, Chivasso et al. [3] and Chikwe et al. [6] compared MV repair to MV replacement for degenerative MV regurgitation in octogenarians and showed on their Kaplan-Meier curve that the reduction of the survival rate in patients who underwent MV replacement was mainly observed within 1 year after surgery. The survival curves for the 2 groups after 1 year were separated but parallel, highlighting the impact of initial excess mortality in the replacement group. Furthermore, previous studies [4,17,18] have reported that the LV ejection fraction after MV repair progressively improved until 1 year of follow-up, whereas there was no significant improvement after MV replacement despite the preservation of the subvalvular apparatus. This is a further explanation of the fact that the overall survival and cardiac-related death remained stable after 1 year postoperatively. After propensity score matching, the overall survival and freedom from cardiac-related death did not show significant differences between the 2 groups. However, the statistical analysis of the results still indicate that MV repair may play an important role in the elderly, because there was a marked trend for better long-term clinical outcomes. Multivariate analysis also showed that MV replacement was an independent risk factor for cardiac-related death (p=0.029).

In contrast with younger patients, elderly patients are likely to undergo surgery not only to improve life expectancy, but also to improve their quality of life. From that perspective, the high proportions of MVREs in the MV replacement group, especially lifelong anticoagulation and CTEB (MV repair, n=16 [10.5%]; MV replacement, n=8 [22.9%]) may be considered an additional risk. Another major concern related with MV repair is the risk of long-term SVD requiring a subsequent reoperation. Although the rate of SVD was higher after MV repair, the rate of reoperation for valve dysfunction during the observational period was identical before and after propensity matching. Moreover, a senior surgeon did not perform annuloplasty in 17 patients undergoing MV repair if the mitral annulus was not dilated. Our current practice includes annuloplasty in all MV repair cases if possible, and it is expected that the improved results of MV repair might further decrease the risks of cardiac death and MVREs.

The present study had limitations that must be noted. First, it was a retrospective, observational study conducted at a single institution. Although we enrolled only patients with primary degenerative MR and performed propensity score matching, selection bias and confounding variables might have affected the study results. Second, the indications for performing MV repair or MV replacement were not precisely defined because of the retrospective nature of the present study. Moreover, the surgical techniques and preferences in MV repair changed over time and varied among the operating surgeons. Finally, the number of patients enrolled in the present study might be too small to draw definitive conclusions, which would require a randomized controlled study with a large cohort.

In conclusion, MV repair might be a reasonable choice for primary degenerative MR in the elderly population if successful repair is possible. The early and long-term clinical outcomes of MV repair may be superior to those of MV replacement, and the rate of MVREs, including reoperation, was similar between the 2 groups. MV replacement was an independent risk factor for cardiac-related death in the multivariable analysis.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

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