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Effect of Recurrent Mitral Regurgitation After Mitral Valve Repair in Patients With Degenerative Mitral Regurgitation

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Background: This study investigated the consequences of recurrent mitral regurgitation (MR) after mitral valve (MV) repair in patients with degenerative MR and risk factors for recurrence.

Methods and Results: From January 1990 to December 2015, 792 patients underwent MV repair due to degenerative MR. Recurrent MR was defined as moderate-to-severe MR on follow-up echocardiography. Mean follow-up duration was 8.71±5.58 years. During the follow-up period, MR recurred in 133 (16.8%) patients, and the MR recurrence-free rate at 20 years was 77.5±2.0%. In the recurrence group, the degree of MR decreased in 8 (6.0%) patients and was aggravated in 46 (34.6%) patients. Recurrent MR was associated with increased mortality and adverse left ventricular (LV) remodeling. Independent risk factors for MR recurrence were MV repair performed before 2000, preoperative atrial fibrillation, high LV end-diastolic dimension (LVEDD), prolapse of the isolated anterior leaflet or multiple segments, and absence of ring annuloplasty. Predictors of MR progression were high LVEDD and repair without artificial chordae implantation.

Conclusions: Recurrent MR after MV repair in patients with degenerative MR showed a tendency to progress and was associated with increased mortality and adverse LV remodeling. Early referral for MV repair before development of atrial fibrillation and LV enlargement may reduce the risk of MR recurrence. Moreover, artificial chordae implantation and ring annuloplasty may assure the long-term durability of MV repair.

Key Words: Mitral regurgitation; Mitral valve; Valvular diseases

For patients with degenerative mitral valve regurgitation (MR) caused by prolapse due to flail leaflet, early surgical correction can improve long-term survival and decrease the risk of late heart failure.[1] Even in asymptomatic patients, early surgical correction is associated with long-term benefits in cardiac-related mortality and cardiac events.[2] Furthermore, mitral repair is preferred to replacement due to its safety and durability in correcting degeneration-induced MR.[3] The current American College of Cardiology/American Heart Association guidelines recommend mitral valve (MV) repair regardless of the location of prolapse for symptomatic patients with severe primary MR or asymptomatic patients with left ventricular (LV) dysfunction.[4] For asymptomatic patients with preserved LV function, MV repair is reasonable if it is performed at a Heart Valve Center of Excellence, with an expected mortality rate of less than 1% and a residual MR rate of less than 5%.[4] Some expert single-surgeon studies have suggested that there is a volume-outcome relationship in MV repair[5] and it is possible that almost all degenerative MVs can be repaired safely with a nearly 100% repair rate at a high-volume reference center.[6,7] Multisurgeon practices have also reported comparable outcomes and demonstrated that recurrent MR after MV repair is associated with late death.[8]

The aims of the present study were to investigate the consequences of recurrent MR after MV repair in patients with degenerative MR and to identify risk factors for recurrence.

Methods

The present retrospective study was approved by the Institutional Review Board of Yonsei University Health System, Severance Hospital. The requirement for patient consent was waived because the study did not change the course of treatment and the study database was designed so that individual patients could not be identified.

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Table 1. Baseline Characteristics and Preoperative Echocardiographic Data for the Entire Cohort and in Patients With and Without Recurrence of MR

Variables	Whole cohort (n=792)	MR recurrence (n=133)	Non-recurrence (n=659)	P value
Males	455 (57.4)	75 (56.4)	380 (57.7)	0.78
Age (years)	52.9±14.1	52.5±14.0	53.0±14.1	0.70
BSA (m^2)	1.86±0.35	1.79±0.41	1.87±0.34	0.06
Hypertension	258 (32.6)	37 (27.8)	221 (33.5)	0.20
Diabetes mellitus	58 (7.3)	5 (3.8)	53 (8.0)	0.08
Chronic kidney disease	75 (9.5)	7 (5.3)	68 (10.3)	0.07
Dialysis	3 (0.5)	0 (0.0)	4 (0.6)	>0.99
COPD	45 (5.7)	5 (3.8)	40 (6.1)	0.29
PAOD	8 (1.0)	1 (0.8)	7 (1.1)	>0.99
CVA	49 (6.2)	5 (3.8)	44 (6.7)	0.20
CAOD	88 (11.1)	15 (11.3)	73 (11.1)	0.95
Recent MI	5 (0.6)	0 (0.0)	5 (0.8)	0.60
Atrial fibrillation	216 (27.3)	47 (35.3)	169 (25.6)	0.02
Permanent pacemaker	3 (0.4)	1 (0.8)	2 (0.3)	0.42
Previous cardiac operation	24 (3.0)	4 (3.0)	20 (3.0)	>0.99
LVEF (%)	66.6±8.4	67.4±7.8	66.4±8.5	0.19
LVEDD (mm)	59.1±7.5	62.4±7.8	59.3±7.4	<0.01
LVESD (mm)	38.9±6.5	40.4±6.7	38.6±6.5	<0.01
LVMI (g/m^2)	137.9±38.4	148.7±40.8	136.4±37.9	0.07
LAVI (mL/m^2)	65.7±36.0	79.3±44.3	63.7±34.3	<0.01
RVSP (mmHg)	39.3±16.9	41.7±18.9	38.9±16.6	0.19

Data for continuous variables are given as the mean ± SD, whereas data for categorical variables are given as n (%). BSA, body surface area; CAOD, coronary artery occlusive disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accidents; LAVI, left atrial volume index; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVMI, left ventricular mass index; MI, myocardial infarction; MR, mitral regurgitation; PAOD, peripheral artery occlusive disease; RVSP, right ventricular systolic pressure.

Patient Characteristics

From January 1990 to December 2015, 1,111 consecutive patients underwent MV repair by 6 experienced surgeons at Severance Cardiovascular Hospital in Seoul, Korea. We excluded 319 patients who had the following conditions: mitral stenosis, concomitant aortic valve surgery or tricuspid valve replacement, and non-degenerative MR, such as that caused by ischemic heart disease, rheumatic heart disease, or endocarditis. Patients who required tricuspid annuloplasty for functional tricuspid regurgitation, a Cox-Maze operation for atrial fibrillation, or coronary artery bypass grafting for coronary artery disease were not excluded from the study. Overall, 792 patients were enrolled and divided into 2 groups according to the presence of recurrent MR during the follow-up period.

Echocardiography

Transthoracic echocardiograms were routinely performed pre- and postoperatively using standard methods. Internal linear dimensions of the LV were acquired in the parasternal long-axis view using 2-dimensional echocardiography (2DE) or the 2DE-guided M-mode approach at end-diastolic and end-systolic phases. LV ejection fraction (LVEF) was calculated using M-mode echocardiography or the biplane disk summation technique (modified Simpson's rule). Left atrial volume was also measured using the biplane disk summation technique (modified Simpson's rule). MR severity was assessed on a scale from 1 to 4 by Doppler echocardiography using specific and supportive signs with quantitative parameters. Grade 1 represented mild regurgitation, Grade 2 represented moderate regurgitation, Grade 3 represented moderate-to-severe regurgitation, and Grade 4 represented severe regurgitation. "Residual MR" was defined as MR that was mild or greater on postoperative echocardiography prior to hospital discharge. "Recurrent MR" was defined as MR that was moderate or severe on follow-up echocardiography after discharge. The location and number of prolapses was determined by a surgeon by direct inspection of the surgical field. Multiple-segment prolapse was defined as leaflet prolapse in 2 or more segments among 6 segments of the MV leaflet.

Follow-up and Data Collection

Pre- and perioperative data were collected prospectively from databases at Severance Cardiovascular Hospital. Follow-up data were collected by reviewing medical records, conducting telephone interviews, and searching the "cause of death" statistics provided by Statistics Korea. The collection of long-term survival data was complete in all patients. The mean (±SD) follow-up duration was 8.71±5.58 years (median 8.01 years; interquartile range [IQR] 4.15–12.70 years). Subsequent echocardiographic follow-up was performed in 86.1% of patients alive at 5 years, in 71.6% of those alive at 10 years, and in 65.2% of those alive at 20 years postoperatively. The mean (±SD) echocardiographic follow-up duration was 5.08±4.95 years (median 3.55 years; IQR 0.96–8.25 years).

Statistical Analysis

Statistical analyses were performed using SPSS for Windows

Table 2. Operative Data for the Entire Cohort and in Patients With and Without Recurrence of MR

	Whole cohort (n=792)	MR recurrence (n=133)	Non-recurrence (n=659)	P value
Surgery before 2000	676 (85.4)	87 (65.4)	589 (89.4)	<0.01
CPB time (min)	107.9±39.8	110.9±44.6	107.3±38.8	0.35
ACC time (min)	73.7±40.8	72.7±31.7	73.9±42.4	0.76
Location of prolapse				<0.01
Anterior leaflet	263 (33.2)	65 (48.9)	198 (30.0)	
Posterior leaflet	456 (57.6)	54 (40.6)	402 (61.0)	
Bileaflet prolapse	73 (9.2)	14 (10.5)	59 (9.0)	
Multiple-segment prolapse	171 (21.6)	35 (26.3)	136 (20.6)	0.15
Concomitant surgical procedure				
Tricuspid annuloplasty	122 (15.4)	26 (19.5)	96 (14.6)	0.15
CABG	62 (7.8)	6 (4.5)	56 (8.5)	0.12
Cox-Maze operation	65 (8.2)	9 (6.8)	56 (8.5)	0.51
Minimal/robotic	61 (7.7)	14 (10.5)	47 (7.1)	0.18
Chordae rupture	540 (68.2)	91 (68.4)	449 (68.1)	0.95
Wedge resection and repair	548 (69.2)	71 (53.4)	477 (72.4)	<0.01
Artificial chordae implantation	290 (36.6)	55 (41.4)	235 (35.7)	0.21
Artificial chordae leaflet				0.02
Anterior leaflet	184 (23.2)	43 (31.3)	141 (21.4)	
Posterior leaflet	96 (12.1)	9 (6.8)	87 (13.2)	
Bileaflets	10 (1.3)	3 (2.3)	7 (1.1)	
Chordae shortening	20 (2.5)	9 (6.8)	11 (1.7)	<0.01
Chordae transfer	2 (0.3)	1 (0.8)	1 (0.2)	0.31
Plication	33 (4.2)	11 (8.3)	22 (3.3)	0.01
Commissuroplasty	12 (1.5)	2 (1.5)	10 (1.5)	>0.99
Sliding annuloplasty	6 (0.8)	1 (0.8)	5 (0.8)	>0.99
Ring annuloplasty	761 (96.1)	115 (86.5)	646 (98.0)	<0.01
Residual MR at OR	42 (5.3)	23 (17.3)	19 (2.9)	<0.01

Data for continuous variables are shown as the mean ± SD, whereas data for categorical variables are given as n (%). ACC, aorta cross clamp; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; MR, mitral regurgitation; OR, operating room.

(release 22.0; SPSS Inc., Chicago, IL, USA). All data are expressed as the mean ± SD or as frequencies and percentages. Continuous variables were compared using Student's t-test, whereas categorical variables were compared using Pearson's Chi-squared test or Fisher's exact test. Postoperative outcomes were compared using these same paired tests. Cox's proportional hazard regression model was used to identify risk factors of overall death, MR recurrence, and MR progression. Long-term survival, MR recurrence rate, or mitral reoperation rate curves were analyzed by the Kaplan-Meier method. The log-rank test was used to compare differences between curves. Statistical significance was set at $P<0.05$.

Results

Baseline characteristics and preoperative echocardiographic data are given in **Table 1**. Isolated anterior leaflet prolapse was observed in 263 (33.2%) patients, isolated posterior leaflet prolapse was observed in 456 (57.6%) patients, and bileaflet prolapse was observed in 73 (9.2%) patients. Multiple-segment prolapse was noted in 171 (21.6%) patients. Wedge resection and repair were performed in 548 (69.2%) patients, and artificial chordae implantation with Gore-Tex (W.L. Gore & Associates, Flagstaff, AZ, USA) was performed in 290 (36.6%) patients. Furthermore, ring annuloplasty was conducted in 761 (96.1%) patients. There were no patients with greater-than-moderate residual MR in the operating room, but 42 (5.3%) patients had mild residual MR in the operating room (**Table 2**).

Early and Long-Term Outcomes

There were 8 (1.0%) in-hospital deaths, and early mortality was similar between the MR recurrence and non-recurrence groups. There were 5 (0.6%) in-hospital reoperations in the recurrence group due to significant residual MR and its related symptoms. During the follow-up period, MR recurred in 133 (16.8%) patients, and there were 107 (13.5%) late deaths and 41 (5.2%) late mitral reoperations (**Table 3**). At 20 years, the overall survival rate was 64.3±4.3%, the freedom from mitral reoperation rate was 94.3±1.1%, and the freedom from recurrent MR rate was 77.5±2.0%.

Clinical Significance of Recurrent MR

In patients with recurrent MR, the initial echocardiographic diagnosis of MR was Grade 2 in 87 patients, Grade 3 in 32 patients, and Grade 4 in 14 patients. At the last follow-up echocardiography, MR was Grade 1 in 5 patients, Grade 2 in 50 patients, Grade 3 in 48 patients, and Grade 4 in 30 patients. Progression of MR was observed in 46 (34.6%) patients, whereas only 8 (6.0%) patients showed an improvement of MR. The severity of MR did not change in 79 (59.4%) patients.

Table 4 lists LVEDD and LVESD values obtained

Table 3. Early and Long-Term Outcomes in the Entire Cohort and in Patients With and Without Recurrence of MR

	Whole cohort (n=792)	MR recurrence (n=133)	Non-recurrence (n=659)	P value
30-day mortality	3 (0.4)	0 (0.0)	3 (0.5)	>0.99
In hospital death	8 (1.0)	1 (0.8)	7 (1.1)	>0.99
In hospital re-operation	5 (0.6)	5 (3.8)	0 (0.0)	<0.01
Residual MR at discharge				
Grade 1	61 (7.7)	23 (17.3)	39 (5.9)	<0.01
Grade 2	23 (2.9)	17 (12.8)	6 (0.9)	
Grade 3	4 (0.5)	4 (3.0)	0 (0.0)	
Grade 4	4 (0.5)	4 (3.0)	0 (0.0)	
Late death	107 (13.5)	32 (18.0)	75 (11.4)	<0.01
Overall death	115 (14.5)	33 (19.3)	82 (12.4)	<0.01
Cardiac-related death	50 (6.3)	16 (8.4)	34 (5.2)	<0.01
Mitral reoperation	41 (5.2)	40 (30.1)	1 (0.2)	<0.01

Data are given as n (%). MR, mitral regurgitation.

Table 4. Echocardiographic Characteristics Before Surgery and at the Last Follow-up in Groups With and Without Recurrence of MR

	LVEDD (mm)	LVESD (mm)	LVEF (%)	LVMI (g/m²)	LAVI (mL/m²)
MR recurrence (n=133)					
Preoperative	62.4±7.8	40.4±6.7	67.4±7.8	148.7±40.8	79.3±44.3
Last follow-up	54.2±7.5	37.2±7.7	61.7±11.4	134.6±107.1	69.6±46.1
Mean difference	8.1±7.7	3.1±6.2	5.8±10.6	10.3±112.8	10.4±32.5
Non-recurrence (n=659)					
Preoperative	59.3±7.4	38.6±6.5	66.4±8.5	136.4±37.9	63.7±34.3
Last follow-up	49.1±5.7	33.7±5.8	61.7±9.4	129.5±466.4	42.4±23.6
Mean difference	10.0±6.9	4.9±5.9	4.6±9.4	6.9±465.6	21.2±24.0
P value[A]	0.006	0.002	0.218	0.966	0.009

Data are given as the mean ± SD. [A]P values are shown for comparisons of the mean differences between the MR recurrence and non-recurrence groups. Mean differences were calculated by subtracting preoperative values from those obtained at the last follow-up. Abbreviations as in Table 1.

preoperatively and at the last follow-up echocardiography in both the recurrent and non-recurrent MR groups. The mean difference in LVEDD was greater in patients without than with recurrent MR (10.04±6.86 vs. 8.14±7.73 mm, respectively; P<0.01). The mean difference in LVESD was also greater in patients without recurrent MR (4.88±5.90 vs. 3.07±6.16 mm; P<0.01). Moreover, these mean differences were significantly correlated with recurrent MR (area under curve [AUC]=0.531 [P=0.03] and AUC=0.576 [P<0.01] for LVEDD and LVESD, respectively), as was the man difference in and left atrial (LA) volume index (AUC=0.584, P=0.02; **Figure S1**).

At 20 years, the long-term survival rate was significantly higher in patients without recurrent MR than in those with recurrent MR (65.9±6.3% vs. 57.0±6.7%, respectively; P=0.045; **Figure S2A**). However, the MR grade at the last follow-up did not affect the survival rate (**Figure S2B**). Multivariate analysis showed that recurrent MR was an independent risk factor for overall death (hazard ratio [HR] 1.61; 95% confidence interval [CI] 1.04–2.51; P=0.04) and mitral reoperation (HR 178.68; 95% CI 18.30–1,744.71; P<0.01; **Table 5**).

Predictors of MR Recurrence

The incidence of preoperative atrial fibrillation was higher in patients with than without recurrent MR (n=169 [25.6%] vs. n=47 [35.3%], respectively; P=0.02). Patients with recurrent MR also had significantly larger LV chamber size and LA volume (**Table 1**). Patients with recurrent MR were more likely to have been operated on prior to 2000 and had a tendency to have isolated anterior leaflet prolapse. Intraoperatively, they were also more likely to have undergone artificial chordae implantation to the anterior leaflet, chordae shortening, and plication. However, they were less likely to have undergone ring annuloplasty and wedge resection and repair. More patients with than without recurrent MR had mild residual MR in the operating room (n=23 [17.3%] vs. n=19 [2.9%]; P<0.01; **Table 2**).

Multivariate analysis showed several predictors of recurrent MR, including: (1) surgery performed before 2000; (2) preoperative atrial fibrillation and high LVEDD; (3) prolapse of the isolated anterior leaflet and multiple segments; (4) absence of ring annuloplasty; and (5) residual MR at discharge (**Table 6**). Patients with MV repair performed before 2000 had a significantly lower freedom from mitral reoperation rate (82.6±3.8% vs. 92.8±2.6%; P<0.01; **Figure S3**) and a lower MR recurrence rate (58.7±4.7% vs.

Table 5. Predictors of Overall Death and Mitral Reoperation

	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	P value	HR (95% CI)
Overall death				
Chronic kidney disease	<0.01	3.49 (1.98–6.13)	<0.01	2.97 (1.64–5.36)
Diabetes mellitus	<0.01	2.57 (1.41–4.70)	0.05	2.02 (1.00–4.07)
Peripheral artery disease	<0.01	5.10 (1.88–13.87)	<0.01	4.15 (1.50–11.51)
Atrial fibrillation	<0.01	3.37 (2.32–4.89)	<0.01	2.93 (1.98–4.35)
Recurrent MR	0.04	1.52 (1.00–2.28)	0.04	1.61 (1.04–2.51)
MV reoperation				
Tricuspid annuloplasty	<0.01	4.66 (2.35–9.27)	<0.01	4.35 (2.16–8.75)
Chordae transfer	0.02	9.98 (1.35–73.81)	<0.01	262.6 (14.9–4,634.9)
Ring annuloplasty	<0.01	0.12 (0.06–0.24)	<0.01	0.37 (0.18–0.75)
Residual MR at discharge	<0.01	9.53 (5.05–17.98)	<0.01	2.65 (1.36–5.15)
Recurrent MR	<0.01	193.0 (26.5–1,404.7)	<0.01	178.7 (18.3–1,744.7)

Data show hazard ratios (HR) with 95% confidence intervals (CI) in parentheses. MR, mitral regurgitation; MV, mitral valve.

Table 6. Predictors of Overall, Early, and Late Recurrent MR

	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	P value	HR (95% CI)
Overall				
Surgery before 2000	<0.01	2.65 (1.85–3.80)	<0.01	2.07 (1.30–3.30)
Atrial fibrillation	<0.01	1.73 (1.21–2.48)	0.01	1.62 (1.12–2.35)
High LVEDD	<0.01	1.04 (1.02–1.07)	0.04	1.02 (1.00–1.05)
Anterior leaflet prolapse	<0.01	2.10 (1.49–2.95)	<0.01	2.03 (1.43–2.88)
Multiple-segment prolapse	0.04	1.48 (1.01–2.17)	<0.01	1.78 (1.19–2.67)
Ring annuloplasty	<0.01	0.22 (0.14–0.36)	<0.01	0.38 (0.20–0.72)
Residual MR at discharge	<0.01	4.83 (3.08–7.58)	<0.01	5.40 (3.70–7.89)
Early				
Minimal or robotic	0.01	2.61 (1.27–5.37)	0.02	2.52 (1.19–5.32)
Wedge resection and repair	<0.01	0.27 (0.16–0.48)	<0.01	0.22 (0.12–0.42)
Chordae shortening	0.01	3.60 (1.30–9.98)	0.05	3.31 (1.00–10.92)
Chordae transfer	0.01	14.8 (2.1–107.3)	<0.01	39.4 (5.2–301.9)
Ring annuloplasty	<0.01	0.21 (0.10–0.48)	<0.01	0.22 (0.08–0.62)
Residual MR at OR	<0.01	4.51 (2.20–9.26)	0.04	2.43 (1.02–5.78)
Late				
Surgery before 2000	<0.01	3.38 (2.17–5.26)	0.04	1.64 (1.03–2.61)
Atrial fibrillation	<0.01	1.99 (1.27–3.13)	0.02	1.57 (1.08–2.29)
High LVEDD	<0.01	1.05 (1.01–1.07)	0.01	1.05 (1.01–1.09)
Anterior leaflet prolapse	<0.01	1.86 (1.21–2.88)	<0.01	2.14 (1.50–3.01)
Ring annuloplasty	<0.01	0.23 (0.12–0.43)	<0.01	0.40 (0.21–0.76)
Residual MR at discharge	<0.01	5.95 (3.65–9.69)	<0.01	2.52 (1.43–4.43)

Data show HR with 95% CI in parentheses. Abbreviations as in Tables 2,5.

84.1±1.7%; P<0.01) at 15 years compared with those undergoing MV repair after 2000 (**Figure A**). Before 2000, MV repair was mostly performed with wedge resection and repair regardless of the location of the prolapse, and chordae manipulation was performed with shortening. After 2000, artificial chordae implantation was performed in a greater number of patients (n=286; 42.3%), and ring annuloplasty was used for almost all patients (n=671; 99.3%). Differences in surgical technique between before and after 2000 are summarized in **Table S1**. The presence of isolated anterior leaflet prolapse was associated with a significantly lower freedom from recurrent MR rate than isolated posterior leaflet prolapse (69.0±3.7% vs. 83.3±2.3%, respectively; P<0.01). The freedom from recurrent MR rate with bileaflet prolapse (72.9±8.0%) was similar to that of isolated anterior leaflet prolapse (P=0.35), but showed a tendency to be lower that that for isolated posterior leaflet prolapse (P=0.051; **Figure B**). The presence of residual MR, even mild, at discharge significantly lowered the freedom from recurrent MR rate (**Figure C**). In addition, high preoperative LVEDD was significantly correlated with recurrent MR (AUC=0.626, optimal cut-off value=61 mm; P<0.01). A high LVEDD (≥61 mm) was associated with a low survival rate at 20 years compared with a low LVEDD (69.7±3.2%

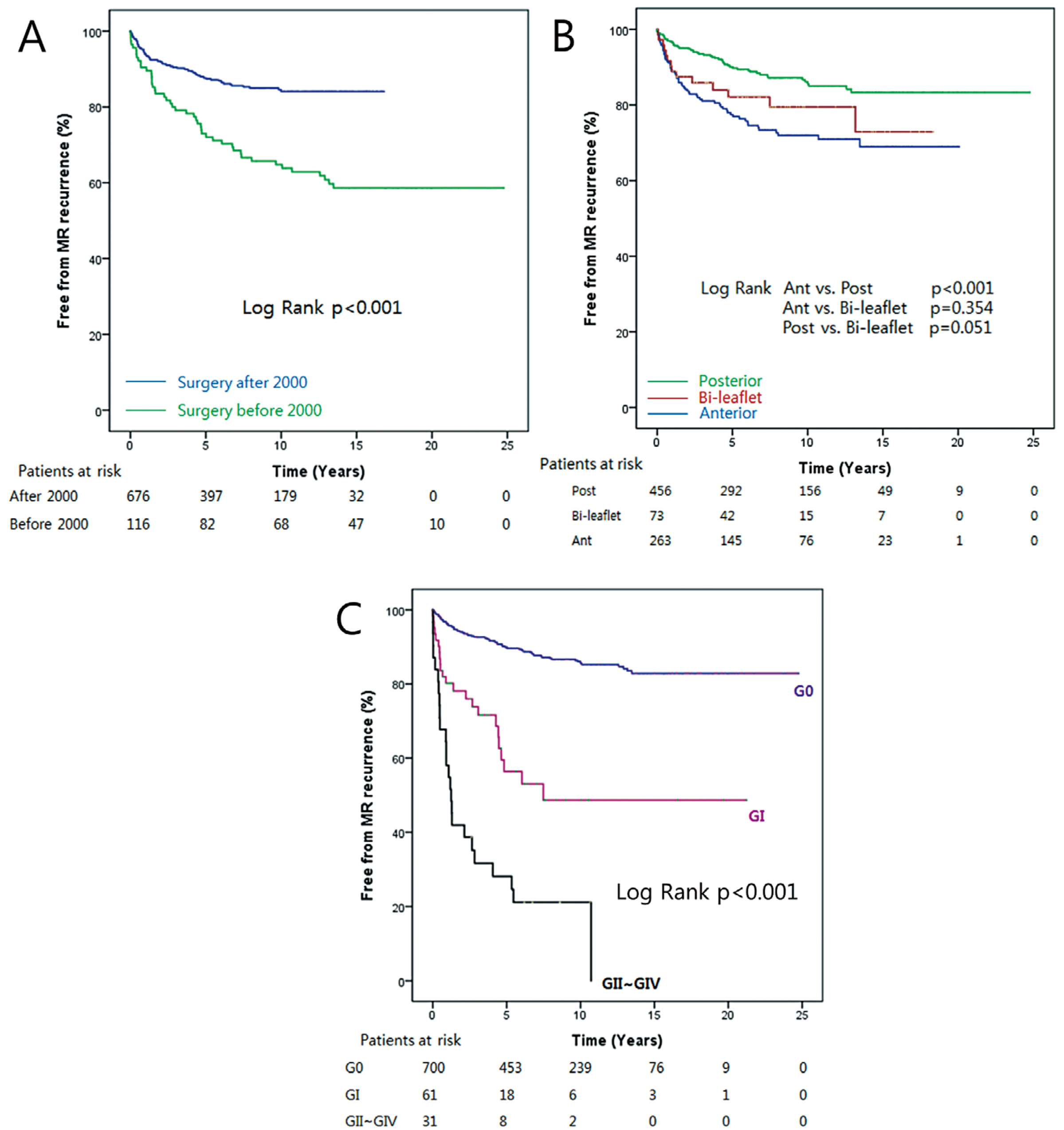

Figure. Freedom from recurrent mitral regurgitation rate in (**A**) patients who underwent surgery before and after 2000, (**B**) patients with isolated anterior (Ant), posterior (Post) or bileaflet prolapse, and (**C**) patients with mild, moderate-to-severe or no residual mitral regurgitation (MR) at discharge. G0, grade 0 (no residual MR); GI, grade 1 MR; GII–IV, grade 2, 3 or 4 MR.

vs. 82.9±2.6%, respectively; P<0.01; **Figure S4**).

Timing of MR Recurrence

Early (<1 year after surgery) and late (≥1 year after surgery) MR recurrence occurred in 51 (38.3%) and 82 (61.6%) patients, respectively. The predictors of early and late recurrence were somewhat different (**Table 6**). The predictors of early recurrence were surgery performed with a minimally invasive procedure, including robotic surgery, without wedge resection and repair, chordae shortening, transfer, absence of ring annuloplasty, and residual MR in the operating room. Predictors of late recurrence were surgery performed before 2000, preoperative atrial fibrillation, high LVEDD, isolated anterior leaflet prolapse, absence of ring annuloplasty, and residual MR at discharge.

Predictors of MR Progression

In patients with residual MR at discharge (n=93), MR progressed in 35 (37.6%) patients. Predictors of MR progression were preoperative high LVEDD and surgery

Table 7. Predictors of Progression of MR in Patients With Residual MR at Discharge and Predictors of Recurrent MR in Those Without Residual MR at Discharge

	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	P value	HR (95% CI)
Progression of MR in patients with residual MR at discharge				
High LVEDD	<0.01	1.05 (1.01–1.09)	<0.01	1.04 (0.01–0.08)
Artificial chordae implantation	<0.01	0.37 (0.20–0.69)	<0.01	0.32 (0.16–0.98)
Recurrent MR in those without residual MR at discharge				
Surgery before 2000	<0.01	3.33 (2.15–5.16)	<0.01	2.55 (1.50–4.32)
Atrial fibrillation	<0.01	2.01 (1.30–3.13)	<0.01	2.10 (1.30–3.40)
High LVEDD	<0.01	1.04 (1.01–1.07)	0.02	1.06 (1.01–1.11)
Anterior leaflet prolapse	<0.01	2.22 (1.45–3.40)	<0.01	2.72 (1.73–4.29)
Multiple-leaflet prolapse	0.02	1.72 (1.08–2.74)	<0.01	2.01 (1.22–3.32)
Ring annuloplasty	<0.01	0.23 (0.12–0.43)	<0.01	0.21 (0.10–0.44)

Data show HR with 95% CI in parentheses. Abbreviations as in Tables 2,5.

without artificial chordae implantation. In those patients without residual MR at discharge (n=699), MR recurred in 85 (12.1%). Predictors of recurrent MR in those without residual MR at discharge were similar to the predictors in the entire whole population: surgery performed before 2000, preoperative atrial fibrillation, high LVEDD, isolated anterior leaflet prolapse, multiple-segment prolapse, and absence of ring annuloplasty (**Table 7**).

Discussion

The present data based on the experiences of many surgeons over a 20-year period revealed 3 main clinical outcomes regarding recurrent MR after MV repair in patients with degenerative MR, as detailed below.

First, recurrent MR after MV repair rarely improved and showed a tendency to progress. The causes of recurrent MR after MV repair have been classified into 2 categories: procedure-related factors and valve-related factors.[9] Procedure-related factors are associated with detachment of the annuloplastic ring, rupture of expanded polytetrafluoroethylene (ePTFE) neochordae, or failure of the initial repair, such as improper length of ePTFE neochordae or leaflet restriction due to improper leaflet resection. Valve-related factors include the progression of degenerative change or endocarditis. The present study analyzed the different factors associated with early and late recurrence. Early recurrence was associated with procedure-related factors, such as minimally invasive surgery, old-fashioned chordae manipulation (shortening or transfer), the absence of wedge resection and repair or ring annuloplasty, and residual MR in the operating room. Late recurrence was mostly associated with valve-related factors, such as preoperative atrial fibrillation, high LVEDD, and isolated anterior leaflet prolapse, which could aggravate valve degeneration. Because late recurrent MR is primarily related to valve-related factors, it tends to progress and is rarely improved by conservative management, including medical treatment. In many cases, it requires aggressive intervention, including repeated surgical correction.

Second, recurrent MR adversely affected LV reverse remodeling. Suri et al[8] also reported that patients with recurrent MR had significantly larger residual LV chamber size and myocardial hypertrophy at their latest follow-up echocardiography. The regurgitation flow from MR overloads the left atrium and LV, thereby leading to dilatation of the LV. Thus, MR-induced remodeling is characterized by higher LV radius : thickness ratios and lower mass : volume ratios.[10] Reverse LA and LV remodeling could occur after early surgical correction of MR,[8,11,12] but the incomplete reduction of MR or late recurrence of MR leads to deterioration of LV function and adversely affects the reverse remodeling of the LA and LV.

Third, recurrent MR significantly increased late deaths. Prior studies analyzing outcomes of MV repair and recurrent MR could not demonstrate a relationship between recurrent MR and the risk of death.[3,5–7,9,12,13] Recently, Suri et al[8] demonstrated that recurrent MR is an independent risk factor for late death (HR 1.72; 95% CI 1.24–2.39; P=0.002). The present study also showed that recurrent MR independently increased late death (HR 1.61; 95% CI 1.04–2.51; P=0.04). In addition, in the present study, the freedom from moderate-to-severe recurrent MR rate was higher than that reported by David et al[7] (69.2% vs. 77.5%), but the freedom from severe recurrent MR rate was lower (90.7% vs. 87.1%). Because the proportion of severe recurrent MR with was higher in the present study than in the study of David et al,[7] recurrent MR could be an independent risk factor for late death, which differs from the findings reported in previous studies.

The independent risk factors for recurrent MR after MV repair found in the present study were surgery performed before 2000, preoperative atrial fibrillation and high LVEDD, prolapse of the anterior leaflet and multiple segments, absence of ring annuloplasty, and residual MR at discharge. Moreover, MV repair performed before 2000 increased the risks of mitral reoperation and recurrent MR. The most important factors that changed after 2000 were surgical techniques for anterior leaflet prolapse and the presence of intraoperative transesophageal echocardiography (TEE). Intraoperative TEE was used after the late 1990s and allowed for the detection of residual MR in the operating room, thus reducing the incidence of incomplete repair. In addition, the surgical strategy for anterior leaflet prolapse changed after 2000 to artificial chordae implantation with ePTFE, and ring annuloplasty was performed in almost all patients. The first report of artificial chordae implantation with ePTFE in humans was that of David.[14] Since then, it has been widely used to repair anterior leaflet prolapse because of its long-term durability and safety.[15,16] The present study shows that after implementation of artificial chordae implantation, the incidence of recurrent MR and mitral reoperation decreased. Despite the wide use of artificial chordae implantation, anterior leaflet or bileaflet prolapse remain known risk factors for recurrent MR after MV repair in both single-surgeon series and large-volume reference centers.[7,8,17] Because of leaflet restrictions followed by anterior leaflet resection, there are limited options to treating anterior leaflet prolapse apart from chordal-based manipulations. The techniques of artificial chordae implantation and length adjustment are difficult and require time and experience for surgeons to become familiar with them and achieve success. Thus, compared with posterior leaflet repair, it may take longer to master anterior leaflet repair. In the present study, the higher percentage of artificial chordae implantation to the anterior leaflet in the MR recurrence group resulted from a higher risk of MR recurrence in patients with anterior leaflet prolapse.

Preoperative atrial fibrillation and high LVEDD were also risk factors for recurrent MR. Long-standing volume overload due to chronic MR can cause progressive LV or LA enlargement and stretching of the myocytes, which leads to decreased contractility and increased LA and LV diastolic pressures. These will then produce symptoms and atrial fibrillation.[18] Previous studies reported that preoperative atrial fibrillation and an enlarged LV increased the risk of recurrent MR and mitral reoperation after MV repair.[13,19,20] These findings are in accord with the current consensus that early repair of MR has more benefits than medical treatment.[1,2]

The present study also analyzed the progression of residual MR after MV repair, which has rarely been reported in previous studies. Because of the long-term durability of the artificial chordae using Gore-Tex, artificial chordae implantation can inhibit recurrent prolapse due to valve degeneration and suppress MR progression. Moreover, an already enlarged LV aggravated the residual MR, and this finding also supports the need for the early repair of MR.

The present study has several limitations. First, its results may have been affected by selection bias or unidentified confounding bias, which are known limitations of retrospective studies. Second, the sample size was relatively small. Third, echocardiographic follow-up was not performed in all patients, and the follow-up period was not sufficiently long enough. Fourth, medications (e.g., β-blockers or renin-angiotensin system inhibitors) can affect LV remodeling after MV repair, but data regarding medications could not be obtained because the old medical records (before the introduction of electronic medical records) did not contain this information. Finally, the study involved a single center, which may limit its generalizability.

Conclusions

The present study shows that mitral repair in patients with degenerative MR can be performed with a low risk of operative death, recurrent MR, and mitral reoperation. Moreover, surgical outcomes improved over time due to advances in techniques. However, recurrent MR after MV repair is a serious problem that is associated with late heart failure, mitral reoperation, and late death. Enlarged LV and preoperative atrial fibrillation are risk factors for recurrent MR, and preoperative high LVEDD was a risk factor for MR progression. So, early referral for MV repair before the development of atrial fibrillation and LV enlargement caused by long-standing volume overload due to chronic MR may reduce the risk of MR recurrence and progression. Isolated anterior leaflet and multiple-segment prolapses were also risk factors for MR recurrence despite the wide use of artificial chordae implantation. However, artificial chordae implantation inhibited MR progression in patients with residual MR. So, artificial chordae implantation in cases of anterior leaflet prolapse and all cases of ring annuloplasty shows promise for the long-term durability of MV repair.

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Supplementary Files

Supplementary File 1

Figure S1. Receiver operating characteristic curve between recurrent MR and mean differences in (**A**) LVEDD, (**B**) LVESD, and (**C**) LAVI.

Figure S2. Overall survival rate (**A**) of patients with recurrent MR compared with patients without recurrent MR and (**B**) according to the grade of recurrent MR at last follow-up echocardiography.

Figure S3. Freedom from mitral reoperation rate in patients who underwent surgery before 2000 compared with those undergoing surgery after 2000.

Figure S4. (**A**) Receiver operating characteristic curve between preoperative LVEDD and recurrent mitral regurgitation and (**B**) freedom from recurrent MR rate in patients with high (≥61 mm) vs. low (<61 mm) preoperative LVEDD.

Table S1. Surgical data before vs. after 2000

Please find supplementary file(s);
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