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Research Article

Remodeling on Lateral Side of Posterior Mitral Leaflet in Recurrent Mitral Regurgitation after Mitral Annuloplasty for Patients with Atrial Functional Mitral Regurgitation

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Objective. The high recurrence rate of mitral regurgitation (MR) in patients with atrial functional mitral regurgitation (AFMR) who underwent mitral annuloplasty (MAP) is reported. However, the mechanism of recurrence is not fully understood and appropriate surgical intervention remains unknown. Herein, we reviewed patients with AFMR who underwent MAP at our institution and investigated the preoperative geometric characteristics of the mitral valve in terms of MR recurrence after surgery. *Methods*. We retrospectively evaluated 20 patients with AFMR who underwent MAP between 2010 and 2022. The mean follow-up period was 3.2 ± 2.3 years. Preoperative three-dimensional transesophageal echocardiography (3D TEE) was available for all patients, and geometric analysis of the mitral valve was performed using the Philips Q-Lab software. *Results*. MR recurred in six patients. The rates of freedom from MR recurrence were 79% and 57% at one and three years, respectively. The lateral portion of the posterior mitral leaflet (PML) in patients with recurrent MR was longer and thicker than that in patients without recurrent MR (length of P1; 10 ± 3 vs. 15 ± 5 mm, $p < 0.01$, length of P2; 11 ± 4 vs. 14 ± 4 mm, $p = 0.23$, length of P3; 8 ± 3 vs. 10 ± 3 mm, $p = 0.13$). *Conclusions*. Patients with remodeling of the lateral portion of PML tended to have recurrent MR after MAP. This factor could indicate progressive remodeling, and MAP alone may not be a sufficient intervention for these patients.

1. Introduction

Long-standing atrial fibrillation causes left atrial enlargement and mitral annulus dilatation, leading to functional mitral regurgitation (MR). In recent studies, its pathology is defined as atrial functional MR (AFMR) [1–3]. Previous studies reported that the recurrence rate of MR in patients who underwent MAP (mitral annuloplasty) for AFMR was between 13 and 20% [4–6]. However, the underlying mechanism for the recurrence of MR after MAP for AFMR remains unclear [7]. The quality of three-dimensional transesophageal echocardiography (3D TEE) has greatly improved in the past decade, and its quality allows 3D TEE to be used to diagnose mitral valve morphology and guide surgical intervention [6–10].

We reviewed patients with AFMR who underwent MAP at our institution and investigated the preoperative geometric characters of the mitral valve with 3D TEE in terms of MR recurrence after MAP for AFMR.

2. Methods

2.1. Patients. MAP for AFMR was performed on 25 patients at Osaka University Hospital between 2010 and 2022. This study reviewed 20 patients whose TEE data were available. The mean patient age was 75 ± 7 years, 14 (60%) were female, and the mean follow-up period was 3.2 ± 2.3 years. All patients had long-standing AF that persisted for more than 1 year. Patients with organic abnormalities of the mitral valve leaflets or subvalvular structures, including degenerative mitral valve disease, low left ventricle ejection fraction (LVEF) (less than 50%), abnormal wall motion of the left ventricle (LV), history of acute myocardial infarction, infectious endocarditis, or rheumatic fever, were excluded from the study.

2.2. Echocardiography. Preoperative and postoperative transthoracic echocardiography (TTE) was performed in all patients, and the LV end-diastolic dimension (LVEDD), LV end-systolic dimension (LVESD), LVEF, and left atrium (LA) dimension were measured. The MR and tricuspid regurgitation (TR) grades on Doppler echocardiography were classified as follows: none, 0; trivial, 1; mild, 2; moderate, 3; severe, 4. Tethering of PML was defined as the immobility of PML in preoperative transthoracic echocardiography. Preoperative 3D TEE was available for all patients, and geometric analysis of the mitral valve was performed using the Philips Q-Lab software (Philips Medical Systems, Andover, MA, USA). The area, length, and thickness of the mitral annulus and leaflet were measured during end-systole. The anterior mitral leaflet (AML) and posterior mitral leaflet (PML) angles were defined as the angles between the annular line and the line joining the anterior or posterior annulus and the coaptation point, respectively. The AML and PML were divided into three parts: lateral A1 and P1, middle A2 and P2, and medial A3 and P3, and the length or thickness of each part was measured. Coaptation height after surgery was measured using postoperative TTE and defined as the length of contact between the AML and PML in the end-systole. Postoperative recurrence on MR was defined as moderate or severe MR on postoperative or follow-up echocardiography.

2.3. Surgical Procedures. Surgery was performed through median sternotomy or right mini-thoracotomy. The mitral valve was approached using the left-sided atrial approach. All patients underwent MAP. After sizing the intercommissural distance and AML size, the size of the annuloplasty ring was selected between the just size and two sizes down size. The ring (Memo-3D, Sorin Biomedica Cardio S.r.I., Saluggia, Italy, or Physio II, Edwards Lifestyle, Irvine, CA, USA) was implanted with $2-0$ Ethibond sutures. If there was a large gap between the AML and PML, anterior mitral leaflet chordal reconstruction, posterior mitral leaflet patch augmentation, edge-to-edge, or cleft closure reconstruction was performed at the discretion of the attending surgeons. All patients underwent concomitant left atrial appendage closure, and those with moderate or severe tricuspid valve regurgitation underwent tricuspid annuloplasty.

2.4. Statistical Analysis. Continuous variables are presented as medians and 95% confidence intervals. Categorical variables were reported as frequencies. All statistical analyses were performed using JMP 16.0 (SAS Inc., Cary, NC, USA). Categorical variables were summarized as frequencies and percentages and compared among groups using chi-square or Fisher's exact tests. Continuous variables were summarized as the mean ± SD or median (interquartile range). All p values for statistical analyses are two-tailed, and statistical significance was set at $p < 0.05$. The Kaplan–Meier analysis was used to calculate the freedom rate from MR recurrence after surgery and the overall survival rate.

2.5. IRB Information. This study was approved by the Osaka University Graduate School of Medicine (reference number: 16105).

3. Results

MR recurrence occurred in six patients; the causes were recurrent functional MR in four patients and detachment of the MAP ring in two. The recurrent functional MR occurred at the lateral portion in three patients and at the medial portion in one patient. In the two patients with detachment of the MAP ring, the MAP ring was detached at the medial portion of AML (Table 1). The freedom rates from MR recurrence were 79%, 71%, and 57% at 1, 2, and 3 years after surgery, respectively. The survival rates 1, 3, and 5 years after surgery were 100%, 100%, and 83%, respectively (Figure 1).

3.1. Characteristics of Patients and Preoperative TTE. Table 2 summarizes the patient characteristics and their preoperative TTE data. No significant differences were observed in sex, body surface area, heart failure symptoms, or comorbidities between patients with and without recurrent MR. LVEDD, LVESD, LVEF, LA dimension, MR grade, TR grade, and tethering of PML were not significantly different between the patients with and without recurrent MR.

3.2. Surgical Outcome. Surgical outcomes are summarized in Table 3. There were no significant differences in the repair technique, type and size of the mitral annuloplasty ring, or concomitant surgery between the patients with and without recurrent MR.

3.3. Preoperative TEE. Table 4 summarizes the geometric analysis of the mitral valve using preoperative 3D TEE and Figure 2 shows the comparison in the geometric analysis of the mitral valve between the typical case with and without recurrent MR. Patients with recurrent MR had a longer circumference of the mitral annulus and a larger area of PML than patients without recurrent MR (circumference of the mitral annulus: 137 ± 11 vs. 124 ± 12 mm, $p = 0.02$, PML area: 797 ± 231 vs. 552 ± 144 mm^2 $p = 0.01$). Particularly, the lateral portion of PML in patients with recurrent MR was longer and thicker than those in patients without recurrent MR (length of P1; 10 ± 3 vs. 15 ± 5 mm, $p < 0.01$, length of P2; 11 ± 4 vs. 14 ± 4 mm, $p = 0.23$, length of P3; 8 ± 3 vs. 10 ± 3 mm, $p = 0.13$, thickness of P1; 2.1 ± 0.5 vs.

Table 1: Details of recurrent mitral regurgitation after mitral annuloplasty.

Case	Details of recurrent MR after MAP
1	Functional MR on the lateral side
2	Functional MR on the lateral side
3	MAP ring detachment at the medial side of AML
4	MAP ring detachment at the medial side of AML
5	Functional MR on the medial side
6	Functional MR on the lateral side

MR, mitral regurgitation; AML, anterior mitral leaflet; MAP, mitral annuloplasty.

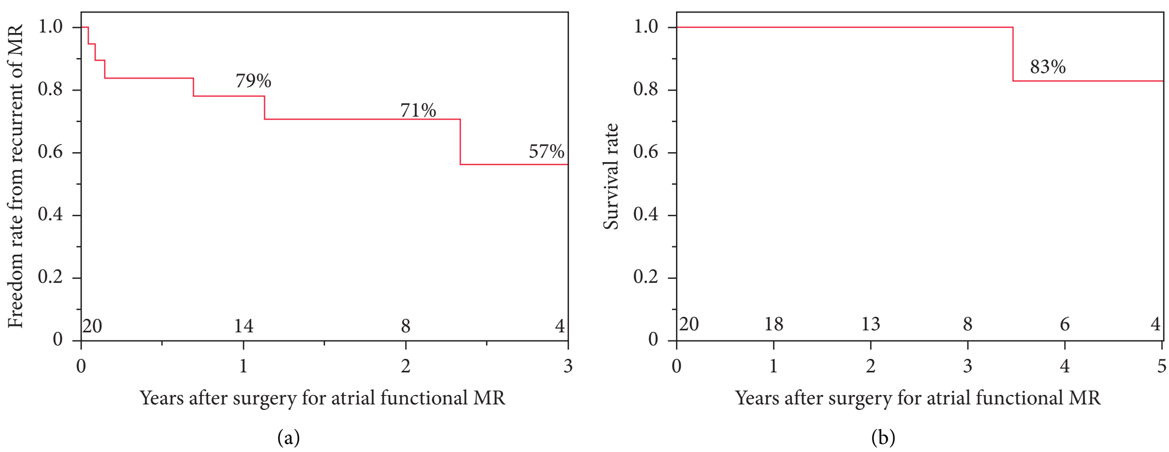

Figure 1: Freedom rate from recurrent mitral regurgitation (a) and survival rate of patients (b) who underwent mitral annuloplasty for atrial functional mitral regurgitation. MR; mitral regurgitation.

Table 2: Patient characteristics and preoperative transthoracic echocardiography data.

	Recurrent MR (−) ($n = 14$)	Recurrent MR (+) ($n = 6$)	p value
Female sex	11 (79%)	3 (50%)	0.201
Age, y	76 ± 7	74 ± 7	0.532
Body surface area, m^2	1.49 ± 0.2	1.55 ± 0.1	0.447
New York heart association class			
II, n (%)	12 (86%)	4 (67%)	0.344
III/IV, n (%)	2 (14%)	2 (33%)	0.344
Comorbidities			
Hypertension	7 (50%)	2 (33%)	0.317
Hyperlipidemia	3 (21%)	1 (17%)	0.689
Diabetes	1 (7%)	1 (17%)	0.596
Chronic kidney disease	5 (36%)	1 (17%)	0.289
Cerebrovascular event	1 (7%)	1 (17%)	0.596
Chronic respiratory disorder	2 (14%)	1 (17%)	1.000
Preoperative TTE			
LVEDD, mm	54 ± 9	55 ± 4	0.681
LVESD, mm	35 ± 6	34 ± 2	0.553
LVEF, %	63 ± 6	68 ± 3	0.078
LA dimension, mm	60 ± 17	67 ± 12	0.358
MR grade	3.5 ± 0.7	3.8 ± 0.4	0.221
TR grade	3.0 ± 1.2	2.3 ± 1.9	0.296
Tethering of PML	5 (36%)	3 (50%)	0.552

MR, mitral regurgitation; TTE, transthoracic echocardiography; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LA, left atrium; TR, tricuspid regurgitation; PML, posterior mitral leaflet.

Table 3: Surgical outcomes of mitral annuloplasty for atrial functional mitral regurgitation.

	Recurrent MR (−) ($n = 14$)	Recurrent MR (+) ($n = 6$)	p value
Repair technique			
Resection and suture	0 (0%)	0 (0%)	
AML chordal reconstruction	2 (14%)	0 (0%)	0.218
PML patch augmentation	1 (7%)	0 (0%)	0.391
Others*	8 (57%)	3 (50%)	0.769
MAP only	4 (29%)	3 (50%)	0.363
Left atrial plication	1 (7%)	1 (17%)	0.515
Mitral annuloplasty ring			
MEMO 3D	13 (93%)	5 (83%)	0.515
Physio II	1 (7%)	1 (17%)	0.515
Mitral annuloplasty ring size	29 ± 3	29 ± 3	0.702
Concomitant surgery			
Maze procedure	1 (7%)	1 (17%)	0.515
PFO closure	2 (14%)	0 (0%)	0.218

Others* included edge to edge and cleft closure. MR, mitral regurgitation; AML, anterior mitral leaflet; PML, posterior mitral leaflet; MAP, mitral annuloplasty; PFO, patent foramen ovale.

Table 4: Geometric analysis of preoperative mitral valve by three-dimensional transesophageal echocardiography.

	Recurrent MR (−) ($n = 14$)	Recurrent MR (+) ($n = 6$)	p value
Mitral annulus			
Anteroposterior diameter, mm	36 ± 5	40 ± 5	0.086
Anterolateral-posteromedial diameter, mm	35 ± 5	41.2 ± 6.5	0.021※
Circumference, mm	124 ± 12	137 ± 11	0.020※
Mitral leaflets			
AML angle, °	13 ± 6	16 ± 6	0.180
PML angle, °	34 ± 12	37 ± 16	0.671
AML area, mm^2	848 ± 168	932 ± 144	0.263
PML area, mm^2	552 ± 144	797 ± 231	0.008※
Length of MV A1, mm	19 ± 5	19 ± 4	0.902
Length of MV A2, mm	27 ± 4	28 ± 4	0.364
Length of MV A3, mm	21 ± 5	24 ± 3	0.282
Length of MV P1, mm	10 ± 3	15 ± 5	0.002※
Length of MV P2, mm	11 ± 4	14 ± 4	0.225
Length of MV P3, mm	8 ± 3	10 ± 3	0.131
Thickness of MV A1, mm	2.0 ± 0.6	2.3 ± 0.5	0.170
Thickness of MV A2, mm	1.9 ± 0.4	2.1 ± 0.4	0.440
Thickness of MV A3, mm	1.9 ± 0.6	2.1 ± 0.4	0.659
Thickness of MV P1, mm	2.1 ± 0.5	3.5 ± 1.0	0.001※
Thickness of MV P2, mm	1.9 ± 0.5	2.7 ± 0.7	0.005※
Thickness of MV P3, mm	2.0 ± 0.5	2.3 ± 0.6	0.204

MR; mitral regurgitation, AML; anterior mitral leaflet, PML; posterior mitral leaflet, MV; mitral valve.

3.5 ± 1.0 mm, $p < 0.01$, thickness of P2; 1.9 ± 0.5 vs. 2.7 ± 0.7 mm, $p < 0.01$, thickness of P3; 2.0 ± 0.5 vs. 2.3 ± 0.6 mm, $p = 0.20$). Regarding the AML and PML angles, there was no significant difference between patients with and without recurrent MR.

3.4. Postoperative Coaptation Height. Patients with recurrent MR had a shorter postoperative coaptation height than patients without recurrent MR (10.0 ± 2.0 vs. 5.1 ± 1.5 mm, $p < 0.01$) (Figures 3 and 4).

4. Discussion

This study showed that (1) patients with recurrent MR after MAP for AFMR had a larger leaflet area on the lateral side of PML than those without recurrent MR after MAP for AFMR. (2) Patients with recurrent MR after MAP for AFMR had a shorter postoperative coaptation height than those without recurrent MR after MAP for AFMR.

Previous studies demonstrated preoperative risk factors for recurrent MR after MAP for AFMR, such as larger LVEDD [4], LVESD [5, 6], and a greater degree of leaflet

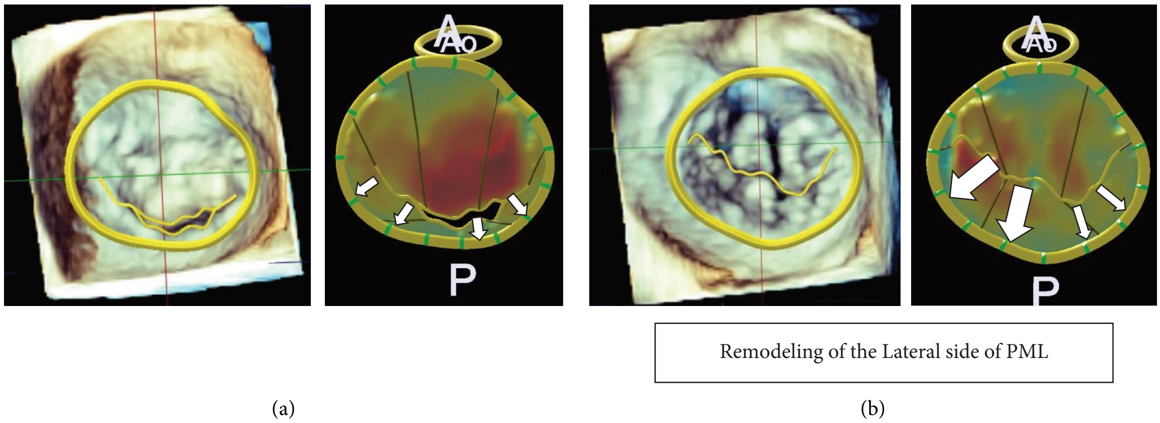

FIGURE 2: Geometric analysis of preoperative mitral valve of patients without (a) and with (b) recurrent mitral regurgitation after mitral annuloplasty for atrial functional regurgitation by three-dimensional transesophageal echocardiography. The white arrows show the remodeling of the posterior mitral leaflet. PML; posterior mitral leaflet.

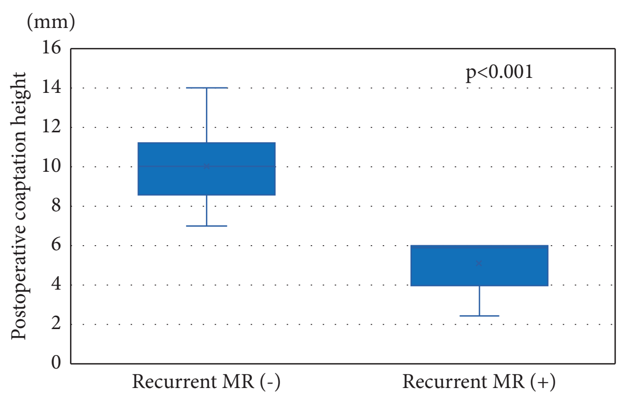

FIGURE 3: A comparison of coaptation height between patients without and with recurrent mitral regurgitation after mitral annuloplasty for atrial functional mitral regurgitation. MR; mitral regurgitation.

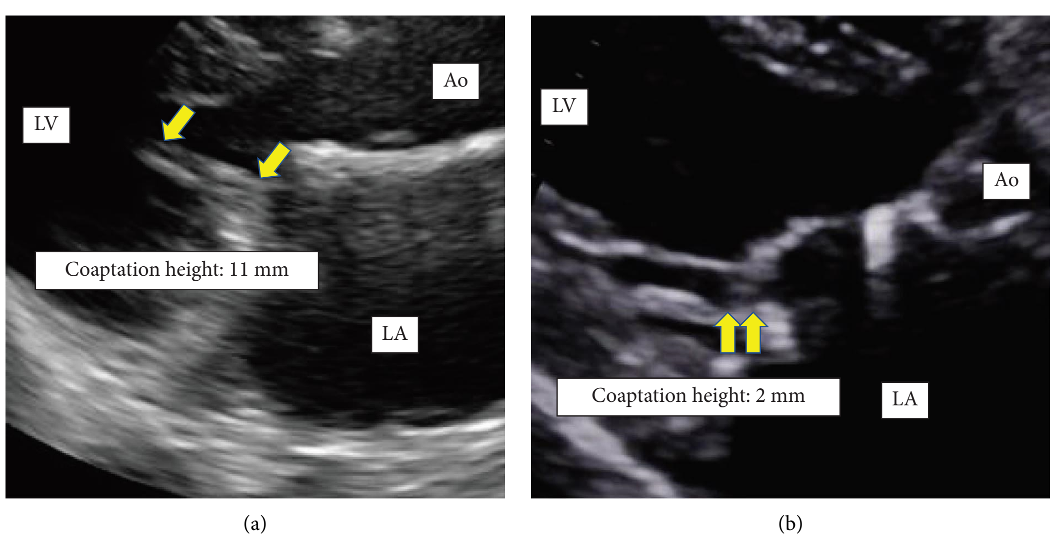

FIGURE 4: Echocardiographic findings on postoperative coaptation height in patients without (a) and with (b) recurrent mitral regurgitation after mitral annuloplasty for atrial functional mitral regurgitation. The yellow arrows show the coaptation range. LV; left ventricle, Ao: aorta, LA; left atrium.

tethering [4] in patients with recurrent MR compared to patients without recurrent MR. However, the risk factors shown in one research were not consistent with those in other studies, and there is still no certain underlying cause for recurrent MR after MAP for AFMR. This could be not only because the AFMRs reported to date have been small studies with few patients, but also because the pathogenesis of AFMR involves multiple factors, including left atrial enlargement due to long-term atrial fibrillation, valve leaflet remodeling and tethering [11, 12]. In addition, this could also be because additional surgical procedures with MAP varied among those studies. In the current study, remodeling of the lateral portion of PML, meaning further remodeling of the lateral portion in PML as a preoperative risk factor, and short coaptation height after MAP as a postoperative one were found. It has previously been shown that postoperative coaptation height after mitral valve repair has a negative correlation with residual MR grade [13]. It would be a unique finding that remodeling of the lateral portion of PML correlated with short coaptation height after MAP for AFMR and led to MR recurrence.

It is an interesting finding that ring detachment was included as a recurrent mode after MAP for AFMR in previous studies [5, 6] and in the present study. It has been reported that mitral annular dilatation and PML area expansion were geometric changes due to AFMR [11, 12, 14] and that functional MR caused cellular changes in the mitral valve leaflet and increased the thickness of the mitral valve [15, 16]. Moreover, it also demonstrated that LA dilatation is caused by the fact that the LA is internal to the posterior mitral annulus and the crest of the LV is external to the posterior mitral annulus in AFMR [17]. In AFMR, pathohistological changes in the mitral valve are found in both the mitral valve leaflet and annulus, and they could cause recurrent functional MR or detachment of the MAP ring in patients with AFMR who underwent MAP. In this study, the recurrent functional MR after MAP tended to occur at the lateral portion, where PML progressed remodeling. The remodeling at the lateral portion of PML might cause less-effective MAP with insufficient coaptation, resulting in recurrent functional MR. It is still unclear if the remodeling of the lateral portion of PML found in the current study would be associated with an advanced stage of pathohistological disorder in the mitral valve with AFMR. Further pathohistological studies are needed to clarify the mechanism and indicate appropriate surgical procedures to improve outcomes in patients with AFMR.

4.1. Limitations. This study has some limitations. This was a retrospective single-center study with a small number of patients in each group. However, we analyzed the high-quality image data in 3D TEE, and this study is informative for cardiovascular surgeons who perform surgery on patients with AFMR.

5. Conclusion

Patients with AFMR with remodeling of the lateral portion of PML tended to have recurrent MR after MAP. This factor could indicate progressive remodeling and an advanced disease stage of AFMR. Thus, MAP alone might not be sufficient for these patients.

Data Availability

The deidentified participant data will not be shared.

Disclosure

This paper was read at the Mitral Conclave of The American Association for Thoracic Surgery in May 5, 2023 [18].

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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