Recurrence of Functional Versus Organic Mitral Regurgitation After Transcatheter Mitral Valve Repair: Implications from Three-Dimensional Echocardiographic Analysis of Mitral Valve Geometry and Left Ventricular Dilation for a Point of No Return

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Background: MitraClip implantation has become the standard transcatheter mitral valve repair (TMVR) technique for severe mitral regurgitation (MR). However, approximately one third of patients have poor outcomes, with MR recurrence at follow-up. The aim of this study was to investigate whether quantitative analysis of mitral valve (MV) geometry on three-dimensional (3D) echocardiography can identify geometric parameters associated with the recurrence of severe functional MR (FMR) versus organic MR (OMR) at 6-month follow-up after TMVR using the MitraClip.

Methods: Sixty-one patients with severe FMR (n = 45) or OMR (n = 16) who underwent transesophageal 3D echocardiography before and 6 months after TMVR were retrospectively analyzed. MV geometry was quantified using 3D echocardiography software. Vena contracta area (VCA) at 6-month follow-up was used to define two outcome groups: patients with good results with VCA < 0.6 cm^2 (MR < 0.6) and those with MR recurrence with VCA ≥ 0.6 cm^2 (MR ≥ 0.6).

Results: MR recurrence was found in 34% of all study patients (21 of 61). In patients with FMR, significant differences between MR < 0.6 and MR ≥ 0.6 were found at baseline for tenting index (1.13 vs 1.23, P = .004), tenting volume (2.8 vs 4.0 ml, P = .04), indexed left ventricular (LV) end-diastolic volume (68.0 vs 99.9 ml/m^2, P = .001), and VCA (0.71 vs 1.00 cm^2, P = .003); no significant parameters of MR recurrence were found in patients with OMR. Multivariate analysis identified indexed LV end-diastolic volume as the strongest independent determinant of MR recurrence. Receiver operating characteristic analysis identified a tenting index of 1.185 (area under the curve 0.79) and indexed LV end-diastolic volume of 88 ml/m^2 (area under the curve 0.76) to best discriminate between MR < 0.6 and MR ≥ 0.6.

Conclusions: MR recurrence after TMVR in patients with FMR is associated with advanced LV dilation and MV tenting before TMVR, which provides clinical implications for a point of no return beyond which progressive LV dilation with MV geometry dilation and tethering cannot be effectively prevented by TMVR. In contrast, no significant determinants of MR recurrence and progressive MV annular dilation could be identified in patients with OMR. (J Am Soc Echocardiogr 2021;■:■-■.)

Keywords: Mitral valve insufficiency, Functional mitral regurgitation, Organic mitral regurgitation, Transcatheter mitral valve repair, Real-time 3D echocardiography, Treatment outcome

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Abbreviations

3D = Three-dimensional

ALPM = Anterolateral-to-posteromedial

AML = Anterior mitral leaflet

AP = Anterior-posterior

APML = Anterior-to-posterior mitral leaflet angle

AUC = Area under the curve

FMR = Functional mitral regurgitation

LV = Left ventricular

LVEDVi = Indexed left ventricular end-diastolic volume

ML = Mitral leaflet

MR = Mitral regurgitation

MV = Mitral valve

MVQ = Mitral valve quantification

NPV = Negative predictive value

OMR = Organic mitral regurgitation

PML = Posterior mitral leaflet

PPV = Positive predictive value

TMVR = Transcatheter mitral valve repair

VCA = Vena contracta area

VCW = Vena contracta width

Mitral regurgitation (MR), which is the most common valve disease (with 2% to 3% of the general population having at least moderate to severe MR),[1] ultimately results in volume overloading of the heart and progressive heart failure.[2] Mitral valve (MV) surgery restores leaflet closure,[3] while transcatheter-based edge-to-edge MV repair has become an accepted alternative in higher-risk patients.[4] However, approximately one-third of transcatheter MV repair (TMVR) patients have poor outcomes (e.g., dyspnea New York Heart Association functional class III or IV, recurrent severe MR at 1-year follow-up).[5,6] Although the mechanism of MR recurrence after TMVR is not completely understood, it is likely to be different from surgical failure[7] because of the fundamentally different repair approaches: rather than annular downsizing,[3] TMVR bridges the leaflets.[4]

Exercise capacity and MR severity are MV repair outcomes,[8,9] but understanding MR recurrence requires measuring MV apparatus geometry, which is possible using transesophageal three-dimensional (3D) echocardiography with advanced MV quantification (MVQ) software.[10,11] MVQ quantifies predictors of surgical repair complexity[12,13]; although there are only limited data for TMVR patients, it has been shown that larger preprocedural mitral annular area predicts ≤50% 24-hour vena contracta area (VCA) reduction[14] and a predominant reduction in annular anterior-posterior (AP) diameter in patients with functional MR (FMR).[15-19] Only limited follow-up data exist after TMVR, but it could be hypothesized that acute AP diameter reduction cannot durably resist annular dilation without stabilization by annuloplasty.

No study has yet investigated the association of MV apparatus geometry on left atrial and left ventricular (LV) dilation and LV function in patients with FMR versus organic MR (OMR) before and at 6-month follow-up after TMVR to understand MR recurrence in FMR and OMR as two fundamentally different MV diseases.

We therefore performed comprehensive 3D echocardiographic MVQ analyses before and 6 months after TMVR, hypothesizing that differences in baseline MV geometry are associated with MR recurrence and can identify a "point of no return" of advanced MV dilation beyond which further progressive annular dilation and MR cannot be effectively prevented or reversed by TMVR.

METHODS

Study Design and Objectives

Of 133 consecutive patients who underwent TMVR using the MitraClip (Abbott Laboratories, Abbott Park, IL) for the treatment of FMR and OMR between March 2009 and February 2014, 61 patients (45 with FMR, 16 with OMR) who had complete 3D echocardiographic data sets acquired within 7 days before TMVR and at 6-month follow-up were retrospectively analyzed. The percentages of patients with FMR (73.8%) and OMR (26.2%) in our study group were similar to the ratio in the total group of 133 consecutive patients (72.3% vs 27.7%) and similar to recent real-world data.[20] Although all patients were scheduled for follow-up transesophageal echocardiography at the university outpatient department, we experienced a relatively high no-show rate because patients were not included in a prospective follow-up study, or patients refused to undergo transesophageal echocardiographic reexamination. Of the 133 consecutive patients, six patients were excluded from our analysis because intraprocedural MR reduction by TMVR was less than one grade or MR grade was >2. All patients were receiving guideline-directed medical therapy at the time of the heart team evaluation as well as after TMVR.[21] The diagnoses of the 16 patients with OMR comprised the following: one with A2 flail, one with P1 flail, five with P2 flail, two with P3 flail, two with posterior mitral leaflet (PML) prolapse, two with anterior mitral leaflet (AML) prolapse, one with bileaflet prolapse, and two with degenerated MVs without prolapse or flail. On the basis of MR severity at follow-up, patients were divided into two groups: those with good TMVR results with VCA $< 0.6\ cm^2$ (MR < 0.6) and those with poor results with MR recurrence with VCA $\geq 0.6\ cm^2$ (MR ≥ 0.6). This VCA cutoff value correlated well with a biplane vena contracta width (VCW) ≥ 0.8 cm,[22] as suggested in current guidelines.[8,9] Intraprocedural MR was graded (1 = mild, 2 = moderate, 3 = severe) according to current guidelines.[8,9,23]

We hypothesized that MV geometric parameters are associated with TMVR outcome. Thus, the following were assessed for FMR and OMR, respectively: (1) identification of baseline differences of MV geometry between the MR < 0.6 and MR ≥ 0.6 groups associated with 6-month outcome, (2) observation of follow-up differences in MV geometry between the MR < 0.6 and MR ≥ 0.6 groups associated with differences in 6-month outcome, (3) identification of differences in MV geometry remodeling between the MR < 0.6 and MR ≥ 0.6 groups, and (4) investigation of the impact of left-heart chamber sizes and function on MV geometry and TMVR outcome.

TMVR was performed under general anesthesia according to established procedural standards.[4] Implantation of more than one MitraClip was performed, if necessary, to achieve an intraprocedural MR reduction of at least one grade or to grade < 2, which is the accepted definition of procedural success,[4] while keeping the mean transmitral pressure gradient ≤5 mm Hg on the basis of intraprocedural echocardiographic monitoring.[24] The study was approved by the institutional committee for human research.

Three-Dimensional Echocardiography

Transesophageal 3D echocardiography at baseline and follow-up was performed under light sedation (2–4 mg midazolam to avoid impaired hemodynamics) using a standard scanner (iE33; Philips Medical Systems, Andover, MA) with a 3D probe (X7-t2). The 3D echocardiographic MV data sets were acquired using live 3D zoom

HIGHLIGHTS

- Recurrence of FMR is determined by LV dilation before MitraClip implantation.
- In patients with FMR, a point of no return of MV tethering exists.
- Remodeling after MitraClip placement is markedly different between FMR and OMR.
- Recurrence of OMR after MitraClip implantation could not be predicted.
- MV remodeling after MitraClip placement can be comprehensively analyzed by 3D echo.

mode and narrowed color Doppler full volume with four to six subvolumes to obtain a color Doppler frame rate of ≥14 volumes/sec. Patients with atrial fibrillation were not excluded.

MR Quantification

MR severity, as quantified by VCA measurement using color Doppler 3D echocardiography, is equally applicable to single, multiple, and asymmetric VCAs.[14,22,25] Baseline VCW was measured in four- and two-chamber view, and their biplane mean was used.[22,26] All VCA measurements using 3D software (QLAB version 9.2; Philips Healthcare, Best, The Netherlands; Figure 1, Supplemental Videos 1–6 available at www.onlinejase.com, Supplemental Figures 1–3) were performed by a single experienced clinician (T.B.). VCAs of multiple jets were summed as previously described.[14] A VCA cutoff of ≥0.6 cm^2, which correlates well with biplane VCW ≥ 0.8 mm, was defined as severe MR.[22]

MV Quantification

MV geometry was assessed using MVQ software (Philips Healthcare), which provides quantitative 3D parameters[10,11] that are not obtainable by two-dimensional echocardiography (Figure 2). Geometric parameters were grouped into the following aspects of the MV apparatus: (1) Annular size was measured by annulus(ALPM) as anterolateral-to-posteromedial annular diameter, annulus(AP) as anterior-to-posterior annular diameter, annulus(area) as the minimum area spanning the saddle-shaped mitral annulus, annulus(circ) as nonplanar annular circumference, annulus(height) as the height of the saddle-shaped annulus, and annulus(ALPM/AP) as the ratio of annulus(ALPM) to annulus(AP) (the mitral annular sphericity index). (2) Leaflet size was measured by ML(area) as exposed total mitral leaflet (ML) area, AML(area) as total AML area including coapting leaflet area, PML(area) as total PML area, PML/AML(area) as the ratio of PML(area) to AML(area), PML/ML(area) as the ratio of PML(area) to ML(area), and AML/ML(area) as the ratio of AML(area) to ML(area). (3) Degree of tenting was determined by tenting(vol) as ML tenting volume, tenting index as the ratio of total ML area (ML(area)) to mitral annular area (annulus(area))—this index being similarly used in earlier studies[27]—and angle(APML) as the anterior to posterior ML angle. (4) Degree of prolapse was measured by prolapse(vol) as the volume of ML prolapse.

Two-Dimensional Echocardiography

Left-heart chamber size and function were assessed using transthoracic two-dimensional echocardiography: LV end-diastolic volume by the biplane summation-of-disks method indexed to body surface area (LVEDVi), LV ejection fraction (LVEF), left atrial volume by the biplane summation-of-disks method indexed to body surface area (LAVi), and LV dP/dt estimated using the time interval between 1 and 3 m/sec on the MR velocity continuous-wave Doppler spectrum.

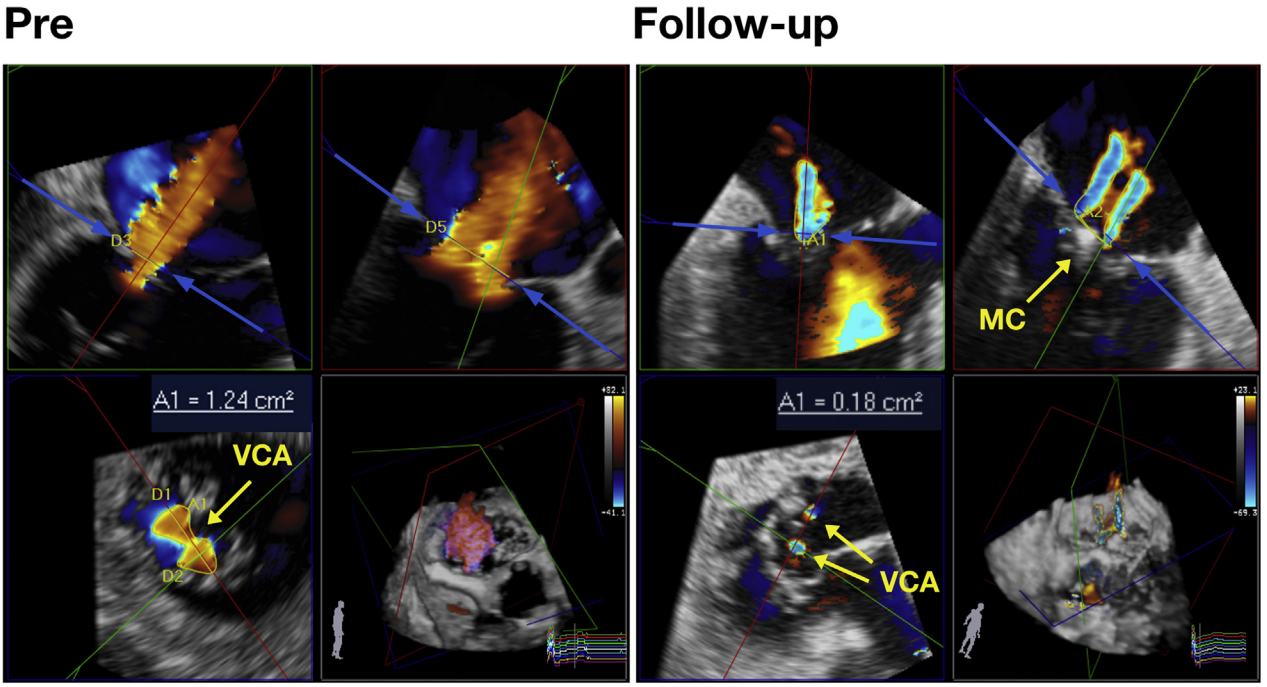

Figure 1 Example of planimetry of VCA. Planimetry of asymmetric VCA (1.24 cm^2) before MitraClip (MC) and at follow-up in the same patient with two VCAs (total of 0.18 cm^2) separated by the MitraClip (MC).

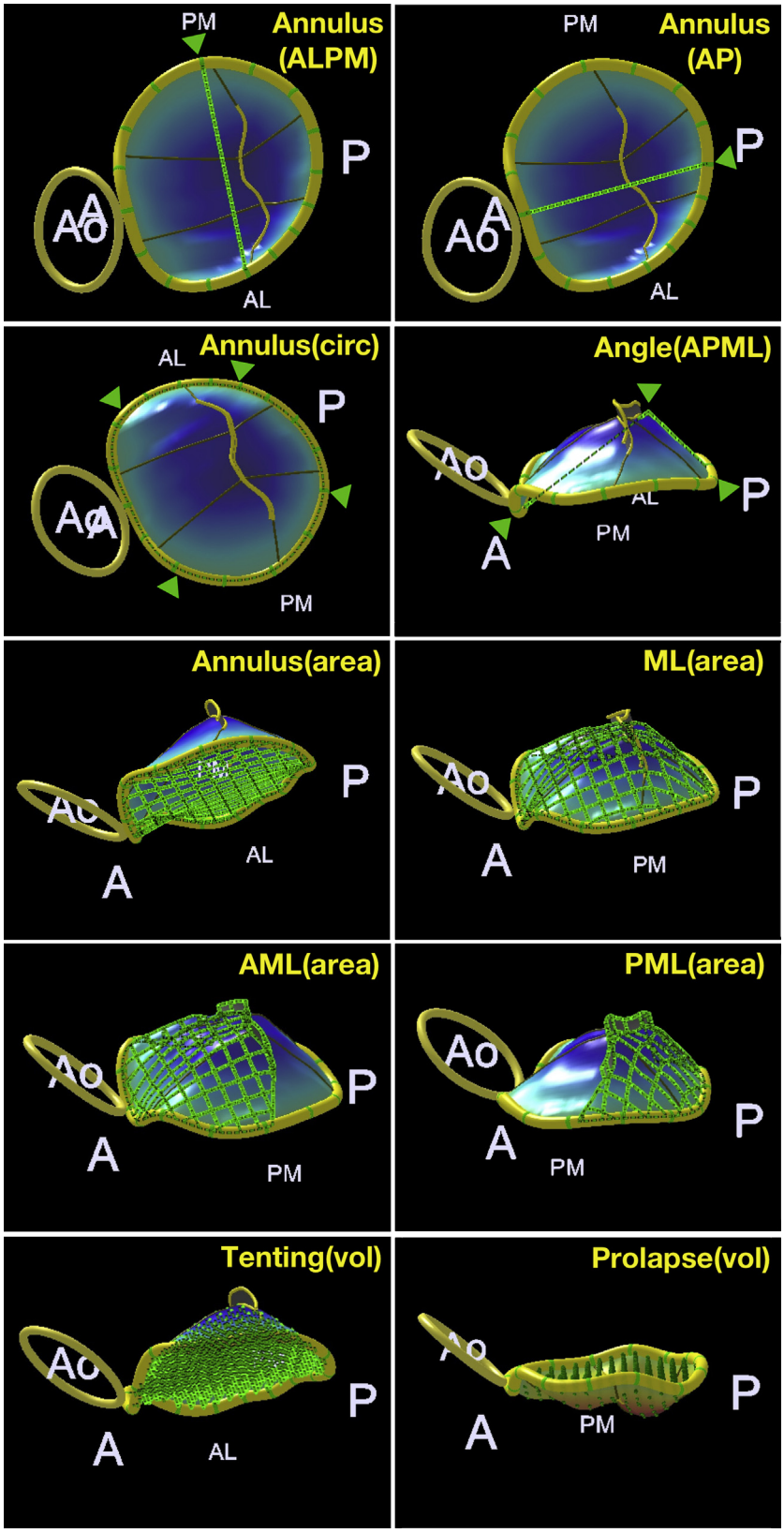

Figure 2 Three-dimensional parameters of MV geometry. Illustration of 3D parameters of MV geometry derived from MVQ analysis. Parameters are indicated by *green lines and grids* (see *green arrows*). *A*, Anterior; *AL*, anterolateral; *Ao*, aorta; *P*, posterior; *PM*, posteromedial.

Table 1 Patient baseline characteristics

	All (n = 61)	FMR (n = 45)	OMR (n = 16)	P
Age, y	73.6 ± 10.7	71.7 ± 11.1	79.0 ± 6.7	**.016**
Gender, male/female	43/18	34/11	9/7	.15
VCA, cm^2	0.77 ± 0.40	0.80 ± 0.41	0.71 ± 0.39	.48
LVEDVi, mL/m^2	73.1 ± 29.7	77.2 ± 30.9	60.7 ± 22.2	.06
LVEF, %	39.6 ± 14.8	36.4 ± 13.9	49.1 ± 13.6	**.003**
LAVi, mL/m^2	62.4 ± 20.8	64.1 ± 20.4	57.5 ± 22.0	.29
Number of clips	1.11	1.07	1.20	.17
Intraprocedural MR grading (0–3) before MitraClip repair	2.8 ± 0.3	2.7 ± 0.4	2.9 ± 0.2	**.013**
Intraprocedural MR grading (0–3) after MitraClip repair	1.5 ± 0.7	1.5 ± 0.7	1.5 ± 0.6	.96

Data are expressed as mean ± SD or as numbers.
LAVi, Left atrial volume; *LVEF*, LV ejection fraction.

Statistical Analysis

Measurements are presented as mean ± SD, and t tests were used to assess differences between groups. Paired t tests were applied to comparisons within study groups between baseline and follow-up. Unpaired t tests were applied to comparisons between the MR < 0.6 and MR ≥ 0.6 groups, which were of different sizes. P values < .05 were considered to indicate statistical significance. Intraobserver and interobserver variability were determined on the basis of actual differences between repeated measurements for MV geometric parameters and VCA, and relative variability was calculated by dividing the absolute difference by the mean of the measurement pair and showed as a percentage. Different linear regression models were fitted to estimate the effects and 95% CIs of the different tenting and LV dilation parameters on study outcome as defined by VCA at 6-month follow-up. Here, VCA at 6-month follow-up was included as a continuous variable. Stepwise model selection was used to identify the most relevant predictor. Receiver operating characteristic and cross-table analysis were performed to determine cutoff values for MR < 0.6 versus MR ≥ 0.6 and to calculate area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Calculations were performed using SPSS version 21 (IBM, Armonk, NY).

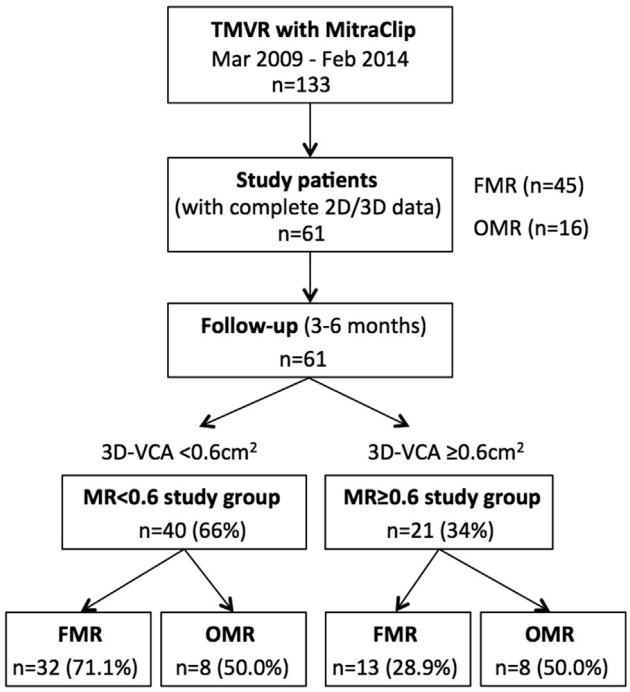

Figure 3 Study design. Overview of study design and characteristics of the two study groups (MR < 0.6 and MR ≥ 0.6).

RESULTS

Intraprocedural MR grading of color Doppler jet size before and after TMVR showed satisfactory MR reduction in all 61 patients (grade 2.75 vs 1.53, with MR reduction to grade < 2 in 38 patients and from grade 3 to grade 2 in 23 patients) independent of MR mechanism (FMR, 2.69 vs 1.52; OMR, 2.93 vs 1.53; Table 1).

MR Quantification

VCA at baseline was 0.77 ± 0.40 cm^2 in the whole study group, with a narrow VCW of 0.63 ± 0.23 cm, a broad VCW of 1.61 ± 0.50 cm, a biplane VCW of 1.12 ± 0.31 cm, and a ratio of broad VCW to narrow VCW of 2.72 ± 1.0, indicating strong asymmetry. At follow-up, VCA was significantly smaller compared with baseline (0.54 ± 0.30 cm^2, P < .0001) with 40 patients (66%) having VCAs < 0.6 cm^2 (mean, 0.36 ± 0.13 cm^2) in the MR < 0.6 group compared with 21 (34%) with VCAs ≥ 0.6 cm^2 (mean, 0.88 ± 0.21 cm^2) in the MR ≥ 0.6 group (Figure 3). Among all patients with FMR, VCA remained significantly smaller at follow-up compared with baseline (P < .001; Table 2); however, 13 of 45 patients (28.9%) had poor results with MR recurrence (i.e., MR ≥ 0.6), whereas among patients with OMR, VCA was not significantly reduced at follow-up compared with baseline (P = .36; Table 2) with eight of 16 patients (50%) having

Table 2 Comparison of measurements in patients with FMR and OMR at baseline versus 6-month follow-up

	FMR			OMR		
	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*
Mitral annulus						
Annulus(ALPM), mm	38.6 ± 4.8	38.5 ± 4.7	.70	**38.6 ± 3.1**	**40.2 ± 4.0**	**.03**
Annulus(AP), mm	32.3 ± 4.1	32.2 ± 4.5	.82	31.3 ± 3.9	32.3 ± 4.1	.28
Annulus(ALPM/AP)	1.20 ± 0.11	1.20 ± 0.12	.89	1.25 ± 0.14	1.26 ± 0.11	.78
Annulus(area), mm^2	1,094 ± 244	1,098 ± 245	.80	1,073 ± 194	1,139 ± 215	.10
Annulus(circ), mm	121.0 ± 14.1	121.3 ± 13.6	.76	120.5 ± 10.5	122.7 ± 11.3	.15
Annulus(height), mm	5.79 ± 1.58	5.56 ± 1.59	.32	5.67 ± 1.55	5.64 ± 1.43	.91
MLs						
ML(area), mm^2	1,264 ± 295	1,251 ± 306	.55	1,207 ± 230	1,261 ± 282	.14
AML(area), mm^2	**845 ± 206**	**796 ± 216**	**.003**	696 ± 130	704 ± 176	.78
PML(area), mm^2	516 ± 136	542 ± 131	.15	**573 ± 170**	**635 ± 196**	**.04**
PML/AML(area)	**0.62 ± 0.14**	**0.71 ± 0.17**	**.003**	0.83 ± 0.25	0.93 ± 0.29	.07
PML/ML(area)	**0.41 ± 0.06**	**0.44 ± 0.07**	**.006**	0.47 ± 0.08	0.50 ± 0.08	.07
AML/ML(area)	**0.67 ± 0.06**	**0.63 ± 0.06**	**.001**	0.58 ± 0.08	0.56 ± 0.09	.12
Tenting						
Tenting(vol), mL	3.2 ± 1.9	3.1 ± 1.9	.41			
Tenting index	**1.16 ± 0.10**	**1.14 ± 0.08**	**.002**			
Angle(APML)	**117.5 ± 18.8**	**120.9 ± 16.8**	**.047**			
Prolapse(vol), mL				1.2 ± 1.0	1.1 ± 1.1	.38
VCA, cm^2	**0.80 ± 0.41**	**0.52 ± 0.29**	**<.001**	0.71 ± 0.39	0.59 ± 0.32	.36
Left ventricle/left atrium						
LVEDVi, mL/m^2	77.2 ± 30.9	76.4 ± 39.2	.78	60.7 ± 22.2	52.5 ± 23.9	.06
LVEF, %	36.4 ± 13.9	34.7 ± 14.7	.26	49.1 ± 13.6	50.4 ± 14.0	.86
LAVi, mL/m^2	64.1 ± 20.4	64.0 ± 20.0	.76	57.5 ± 22.0	60.2 ± 27.1	.91
LV dP/dt, mm Hg/sec	**853 ± 384**	**715 ± 208**	**.03**	1,244 ± 514	999 ± 644	.81

Data are expressed as mean ± SD.
LAVi, Left atrial volume index; *LVEF*, LV ejection fraction.

poor results (i.e., MR ≥ 0.6). All patients in the recurrent MR group (i.e., MR ≥ 0.6) had worsening of MR between the intraprocedural result and 6-month follow-up. No overrepresentation of poor results was found in the five non-EVEREST (Endovascular Valve Edge-to-Edge Repair Study) cases (one with P1 flail [MR ≥ 0.6], two with P3 flail [MR < 0.6 in both], and degenerative MR without prolapse or flail [one with MR < 0.6, one with MR ≥ 0.6]). At baseline, VCA was significantly larger for MR ≥ 0.6 versus MR < 0.6 (1.00 ± 0.40 vs 0.71 ± 0.39 cm^2, $P = .003$) only in patients with FMR (Table 3). At follow-up, VCA was significantly larger for MR ≥ 0.6 versus MR < 0.6 in both patients with FMR and those with OMR (Table 3). However, only in the MR < 0.6 subgroup of patients with FMR was a significant reduction of VCA from baseline to follow-up found (Table 4).

MV Geometry

Table 2 shows significant differences in MV geometric parameters at follow-up versus baseline between patients with FMR and those with OMR. The minor but significant decrease of the tenting index (1.14 ± 0.08 vs 1.16 ± 0.10, $P = .002$) in patients with FMR indicated a reduction of leaflet tethering. AML(area) decreased after TMVR (796 ± 216 vs 845 ± 206 mm^2, $P = .003$) in patients with FMR compared with an increase of PML(area) (635 ± 196 vs 573 ± 170 mm^2, $P = .04$) in those with OMR. Accordingly, AML/ML(area) decreased in patients with FMR, while PML/ML increased in those with OMR. An increase of annulus(ALPM) at follow-up was found only in patients with OMR.

Furthermore, the tenting parameters of tenting index and tenting(vol) were larger at baseline in patients with FMR in the MR ≥ 0.6 group compared with the MR < 0.6 group, indicating greater leaflet tethering (Table 3). The other MV geometric parameters, including those indicating MV annular size and ellipticity, did not differ significantly between MR < 0.6 and MR ≥ 0.6. Compared with patients with FMR, no significant differences in MV geometric parameters were observed between the groups with MR < 0.6 and MR ≥ 0.6 among patients with OMR at baseline. At follow-up, the tenting parameters of tenting index and tenting(vol) in patients with FMR were significantly larger for MR ≥ 0.6 versus MR < 0.6, whereby in patients with OMR, annulus(ALPM) and annulus(circ) were significantly larger for MR ≥ 0.6 versus MR < 0.6, indicating MV annular dilation (Table 3). In patients with OMR, we also found prolapse(vol)

Table 3 Comparison of measurements between MR < 0.6 and MR ≥ 0.6 subgroups at baseline and 6-month follow-up

	MR < 0.6, BL	MR ≥ 0.6, BL	*P*	MR < 0.6, FU	MR ≥ 0.6, FU	*P*
FMR						
Mitral annulus						
Annulus(ALPM), mm	38.7 ± 5.3	38.6 ± 3.5	.95	38.2 ± 4.8	39.2 ± 4.3	.50
Annulus(AP), mm	32.3 ± 4.3	32.4 ± 3.6	.90	31.6 ± 4.7	33.8 ± 3.5	.14
Annulus(ALPM/AP)	1.20 ± 0.10	1.20 ± 0.11	.85	1.22 ± 0.13	1.16 ± 0.10	.17
Annulus(area), mm^2	1,104 ± 265	1,069 ± 191	.68	1,074 ± 250	1,159 ± 228	.29
Annulus(circ), mm	121.5 ± 15.4	120.6 ± 10.8	.85	119.9 ± 13.7	124.7 ± 13.3	.30
Annulus(height), mm	5.85 ± 1.37	5.64 ± 2.06	.69	5.62 ± 1.66	5.42 ± 1.46	.70
MLs						
ML(area), mm^2	1,245 ± 306	1,313 ± 272	.49	**1,190 ± 287**	**1,400 ± 309**	**.04**
AML(area), mm^2	830 ± 221	880 ± 165	.47	759 ± 216	888 ± 194	.07
PML(area), mm^2	521 ± 135	505 ± 143	.72	525 ± 123	585 ± 145	.16
PML/AML(area)	0.65 ± 0.15	0.57 ± 0.12	.13	0.72 ± 0.18	0.67 ± 0.14	.30
PML/ML(area)	**0.42 ± 0.07**	**0.38 ± 0.05**	**.047**	0.45 ± 0.07	0.42 ± 0.06	.18
AML/ML(area)	0.67 ± 0.06	0.67 ± 0.05	.66	0.63 ± 0.06	0.64 ± 0.05	.82
Tenting						
Tenting(vol), mL	**2.8 ± 1.9**	**4.0 ± 1.9**	**.04**	**2.6 ± 1.7**	**4.4 ± 2.1**	**.003**
Tenting index	**1.13 ± 0.09**	**1.23 ± 0.10**	**.004**	**1.11 ± 0.06**	**1.20 ± 0.09**	**<.001**
Angle(APML)	121.5 ± 15.3	110.4 ± 23.0	.06	123.9 ± 16.7	113.5 ± 15.1	.06
VCA, cm^2	**0.71 ± 0.39**	**1.00 ± 0.40**	**.003**	**0.38 ± 0.14**	**0.89 ± 0.22**	**<.001**
Left ventricle/left atrium						
LVEDVi, mL/m^2	**68.0 ± 23.5**	**99.9 ± 36.1**	**.001**	**61.9 ± 20.3**	**112.2 ± 51.2**	**<.001**
LVEF, %	38.3 ± 12.1	31.6 ± 17.6	.14	36.4 ± 14.1	30.5 ± 16.0	.23
LAVi, mL/m^2	63.9 ± 20.1	64.6 ± 21.9	.92	62.6 ± 19.2	67.5 ± 22.3	.46
LV dP/dt, mm Hg/sec	**942 ± 422**	**648 ± 146**	**.04**	760 ± 224	630 ± 149	.11
OMR						
Mitral annulus						
Annulus(ALPM), mm	37.2 ± 2.6	40.1 ± 3.1	.06	**37.5 ± 2.9**	**42.9 ± 2.9**	**.002**
Annulus(AP), mm	31.4 ± 3.9	31.2 ± 4.2	.92	30.7 ± 4.4	33.8 ± 3.5	.13
Annulus(ALPM/AP)	1.19 ± 0.11	1.30 ± 0.15	.13	1.24 ± 0.14	1.27 ± 0.09	.51
Annulus(area), mm^2	1,024 ± 169	1,122 ± 215	.33	1,019 ± 198T	1,227 ± 192	.052
Annulus(circ), mm	117.4 ± 9.3	123.6 ± 11.3	.25	**117.1 ± 10.1**	**128.2 ± 10.1**	**.04**
Annulus(height), mm	5.10 ± 1.34	6.24 ± 1.62	.15	5.36 ± 1.58	5.93 ± 1.31	.45
MLs						
ML(area), mm^2	1,158 ± 215	1,256 ± 249	.41	1,141 ± 296	1,380 ± 223	.09
AML(area), mm^2	700 ± 140	692 ± 129	.91	683 ± 216	725 ± 137	.65
PML(area), mm^2	529 ± 140	617 ± 194	.31	**521 ± 137**	**749 ± 184**	**.014**
PML/AML(area)	0.77 ± 0.19	0.90 ± 0.29	.31	0.81 ± 0.23	1.06 ± 0.30	.08
PML/ML(area)	0.46 ± 0.07	0.48 ± 0.09	.50	0.46 ± 0.07	0.54 ± 0.08	.06
AML/ML(area)	0.61 ± 0.07	0.56 ± 0.08	.22	0.59 ± 0.08	0.53 ± 0.08	.14
Prolapse(vol), mL	0.6 ± 0.5	1.5 ± 1.0	.08	**0.4 ± 0.5**	**1.5 ± 1.1**	**.047**
VCA, cm^2	0.66 ± 0.38	0.76 ± 0.41	.63	**0.32 ± 0.10**	**0.87 ± 0.21**	**<.001**
Left ventricle/left atrium						
LVEDVi, mL/m^2	64.7 ± 27.8	56.2 ± 14.3	.48	61.4 ± 30.6	43.6 ± 10.1	.14
LVEF, %	**40.5 ± 13.5**	**59.0 ± 2.7**	**.003**	44.8 ± 16.7	56.1 ± 8.4	.11
LAVi, mL/m^2	57.2 ± 24.6	57.8 ± 20.6	.97	59.0 ± 22.3	61.4 ± 32.7	.86
LV dP/dt, mm Hg/s	967 ± 205	1,474 ± 595	.11	1,087 ± 894	882 ± 109	.72

Data are expressed as mean ± SD.
BL, Baseline; *FU*, follow-up; *LAVi*, Left atrial volume index; *LVEF*, LV ejection fraction; *MR < 0.6*, without recurrence of severe MR at 6-month follow-up; *MR ≥ 0.6*, with recurrence of severe MR at 6-month follow-up.

Table 4 Comparison of differences of measurements between baseline and 6-month follow-up in MR < 0.6 versus MR ≥ 0.6 subgroups

	MR < 0.6, ΔBL-FU	*P*	MR ≥ 0.6, ΔBL-FU	*P*	*P*, ΔMR < 0.6 vs ΔMR ≥ 0.6
FMR					
Mitral annulus					
Annulus(ALPM), mm	0.50 ± 2.96	.34	−0.65 ± 2.83	.42	.24
Annulus(AP), mm	0.72 ± 2.77	.18	−1.34 ± 2.79	.11	**.029**
Annulus(ALPM/AP)	−0.02 ± 0.12	.46	0.03 ± 0.12	.35	.24
Annulus(area), mm^2	29.9 ± 103.8	.11	**−89.8 ± 123.6**	**.02**	**.002**
Annulus(circ), mm	1.55 ± 5.49	.11	−4.86 ± 6.48	.052	**.002**
Annulus(height), mm	0.23 ± 1.34	.35	0.22 ± 1.93	.68	1.00
MLs					
ML(area), mm^2	**55.0 ± 130.0**	**.02**	−87.0 ± 176.1	.10	**.005**
AML(area), mm^2	**71.7 ± 103.5**	**<.001**	−8.0 ± 89.1	.75	**.02**
PML(area), mm^2	−3.8 ± 113.1	.85	**−80.0 ± 116.4**	**.03**	**.048**
PML/AML(area)	**−0.08 ± 0.19**	**.03**	**−0.09 ± 0.13**	**.02**	.84
PML/ML(area)	−0.03 ± 0.07	.08	**−0.04 ± 0.05**	**.03**	.63
AML/ML(area)	**0.03 ± 0.08**	**.02**	**0.04 ± 0.05**	**.02**	.87
Tenting					
Tenting(vol), ml	**0.4 ± 1.0**	**.047**	−0.4 ± 1.2	.23	**.03**
Tenting index	**0.02 ± 0.08**	**.04**	0.02 ± 0.06	.23	.87
Angle(APML)	−2.39 ± 11.3	.24	−3.11 ± 13.1	.41	.85
VCA, cm^2	**0.34 ± 0.38**	**<.001**	0.11 ± 0.36	.31	.07
Left ventricle/left atrium					
LVEDVi, mL/m^2	**6.1 ± 12.1**	**.007**	−12.3 ± 26.6	.12	**.002**
LVEF, %	2.0 ± 9.4	.25	1.0 ± 11.7	.76	.78
LAVi, mL/m^2	0.1 ± 18.4	.97	−3.0 ± 13.2	.43	.58
LV dP/dt, mm Hg/sec	**246 ± 388**	**.03**	13 ± 184	.99	.12
OMR					
Mitral annulus					
Annulus(ALPM), mm	−0.30 ± 1.72	.64	**−2.79 ± 2.66**	**.02**	**.04**
Annulus(AP), mm	0.76 ± 2.83	.47	**−2.58 ± 2.90**	**.04**	**.04**
Annulus(ALPM/AP)	−0.04 ± 0.09	.20	0.02 ± 0.17	.69	.32
Annulus(area), mm^2	4.6 ± 105.8	.91	**−104.4 ± 94.0**	**.02**	**.047**
Annulus(circ), mm	0.29 ± 5.94	.89	**−4.60 ± 4.67**	**.03**	.09
Annulus(height), mm	−0.26 ± 0.87	.42	0.31 ± 0.73	.27	.17
Mitral annulus					
ML(area), mm^2	16.5 ± 138.6	.75	**−124.3 ± 106.8**	**.01**	**.04**
AML(area), mm^2	17.2 ± 128.0	.71	−32.8 ± 85.4	.31	.37
PML(area), mm^2	7.2 ± 61.6	.75	**−131.9 ± 112.8**	**.01**	**.01**
PML/AML(area)	−0.04 ± 0.12	.43	−0.16 ± 0.25	.11	.23
PML/ML(area)	−0.01 ± 0.04	.69	−0.06 ± 0.08	.08	.14
AML/ML(area)	0.01 ± 0.04	.42	0.03 ± 0.06	.22	.57
Prolapse(vol), ml	0.22 ± 0.34	.22	0.00 ± 0.32	1.00	.27
VCA, cm^2	0.34 ± 0.43	.06	−0.11 ± 0.49	.56	.07
Left ventricle/left atrium					
LVEDVi, mL/m^2	3.3 ± 13.7	.52	**11.8 ± 12.7**	**.049**	.24
LVEF, %	−4.4 ± 14.0	.41	3.8 ± 8.5	.28	.20
LAVi, mL/m^2	−1.8 ± 8.7	.58	0.7 ± 29.6	.95	.82
LV dP/dt, mm Hg/sec	−381 ± 978	.57	**194 ± 256**	**.046**	.38

Data are expressed as mean ± SD.

BL, Baseline; *FU*, follow-up; *LAVi*, Left atrial volume index; *LVEF*, LV ejection fraction; *MR < 0.6*, without recurrence of severe MR at 6-month follow-up; *MR ≥ 0.6*, with recurrence of severe MR at 6-month follow-up.

and PML(area) to be significantly larger in the MR ≥ 0.6 versus MR < 0.6 group, indicating that the increased MV size predominantly affected the PML region.

Analysis of MV remodeling from baseline to follow-up revealed decreases in the tenting parameters of tenting index and tenting(vol) in MR < 0.6 patients with FMR, indicating a significant decrease in leaflet tethering (Table 4). In the MR ≥ 0.6 patients with FMR, only annulus(area) increased from baseline to follow-up, whereas in patients with OMR, nearly all parameters of MV annular dilation increased significantly (Table 4). Comparing differences of MV remodeling between MR < 0.6 and MR ≥ 0.6, we found significant differences in patients with FMR with decreases in MV annular size and tenting in the MR < 0.6 group compared with increases in annulus(AP), annulus(circ), annulus(area), ML(area), and tenting(vol) in the MR ≥ 0.6 group. In patients with OMR, differences in MV remodeling between MR < 0.6 and MR ≥ 0.6 were more strongly related to the increase of MV annular diameters annulus(ALPM) and annulus(AP) and the increases in annulus(area) and ML(area). Analysis of AML and PML leaflet sizes from baseline to follow-up revealed a decrease in AML(area) in the MR < 0.6 FMR group, while PML(area) remained similar. In contrast, PML(area) and PML/ML(area) increased from baseline to follow-up in the MR ≥ 0.6 group, while AML(area) remained similar. However, only an increase in PML(area) was found in the MR ≥ 0.6 OMR group.

Quantification of LV and Left Atrial Size and Function

Analyzing the FMR and OMR patient groups revealed no significant changes in LVEDVi, LAVi, and LVEF between baseline and follow-up (Table 2). Only in patients with FMR was LV dP/dt significantly reduced at follow-up. Comparing MR ≥ 0.6 with MR < 0.6 at baseline, LVEDVi was significantly larger for MR ≥ 0.6 versus MR < 0.6 among patients with FMR (99.9 ± 36.1 vs 68.0 ± 23.5 ml/m^2, $P = .001$), and LV dP/dt was significantly reduced (648 ± 146 vs 942 ± 422 mm Hg/sec, $P = .04$), which may potentially be associated with poor TMVR outcome (Table 3). In patients with OMR, only LVEF was significantly larger for MR ≥ 0.6 versus MR < 0.6 (Table 3). At follow-up among patients with FMR, not only was LVEDVi found to be significantly larger in the MR ≥ 0.6 group compared with the MR < 0.6 group (Table 3), but there was also a larger increase from baseline to follow-up (99.9 ± 36.1 vs 112.2 ± 51.2 ml/m^2); furthermore, the difference between the LVEDVi decrease in the MR < 0.6 group and the increase in the MR ≥ 0.6 group was significant (Δ6.1 ± 12.1 ml/m^2 vs Δ−12.3 ± 26.6 ml/m^2, $P = .002$; Table 4). Compared with this, we found a significant decrease in LVEDVi in the MR ≥ 0.6 patients with OMR.

Observer Variability

Intra- and interobserver variability was determined in 20 study patients, including 15 patients with FMR and five with OMR, and 17 data sets acquired before TMVR and three at follow-up. Repeated 3D measurements were performed on the same volume of the cardiac cycle. Intraobserver variability of VCA measurements was 0.04 ± 0.08 cm^2 (9.2 ± 10.9%), whereas interobserver variability was 0.03 ± 0.06 cm^2 (6.0 ± 7.0%). Intra- and interobserver variability values, respectively, for MV geometric parameters were as follows: annulus(ALPM), 0.3 ± 0.9 mm (1.5 ± 2.2%) and 0.8 ± 1.1 mm (2.4 ± 2.9%); annulus(AP), −0.3 ± 0.9 mm (1.6 ± 2.4%) and −0.3 ± 1.5 mm (3.0 ± 3.6%); annulus(area), 8.8 ± 33.7 mm^2 (2.4 ± 1.6%) and 30.4 ± 58.4 mm^2 (5.0 ± 4.0%); annulus(circ), 1.3 ± 2.4 mm (1.8 ± 1.1%) and −1.1 ± 3.6 mm (2.4 ± 2.1%); annulus(height), 0.4 ± 0.8 mm (12.8 ± 12.1%) and −0.5 ± 1.0 mm (18.6 ± 16.3%); ML(area), −9.8 ± 44.1 mm^2 (2.8 ± 1.6%) and −27.7 ± 61.0 mm^2 (4.1 ± 3.4%); AML(area), −3.2 ± 34.7 mm^2 (3.4 ± 2.9%) and −18.5 ± 59.0 mm^2 (6.4 ± 4.0%); PML(area), −2.8 ± 48.8 mm^2 (7.0 ± 5.7%) and 18.7 ± 64.3 mm^2 (9.4 ± 6.1%); tenting(vol), 0.1 ± 0.5 ml (14.2 ± 16.1%) and −0.4 ± 0.5 ml (17.6 ± 18.5%); angle(APML), −5.5 ± 8.3 (5.5 ± 6.1%) and 2.9 ± 13.1 (9.9 ± 4.5%); and prolapse(vol), −0.00 ± 0.2 ml (29.6 ± 20.9%) and −0.1 ± 0.2 ml (32.9 ± 19.2%).

Cutoff Values for a "Point of No Return" of Progressive MV Tethering in Patients with FMR

As significantly larger LVEDVi, larger VCA, and larger tenting parameters (i.e., tenting index and tenting(vol)) at baseline were associated with MR recurrence (MR ≥ 0.6) in patients with FMR (Table 3), the receiver operating characteristic analysis was performed only in patients with FMR to determine a point of no return of progressive MV tethering. Receiver operating characteristic analysis identified the following as optimal cutoff values to determine progressive LV dilation and MR recurrence: 88 ml/m^2 for LVEDVi (sensitivity 81.3%, specificity 69.2%, AUC 0.76, PPV 86.7%, NPV 60.0%; Figure 4), 0.85 cm^2 for VCA (sensitivity 75.0%, specificity 61.5%, AUC 0.70, PPV 82.8%, NPV 50.0%), 1.185 for tenting index (sensitivity 84.4%, specificity 69.2%, AUC 0.79, PPV 87.1%, NPV 64.3%), and 3.75 ml for tenting(vol) (sensitivity 68.8%, specificity 53.9%, AUC 0.67, PPV 78.6%, NPV 41.2%), whereby the cutoff values for tenting index and LVEDVi were the most sensitive to predict MR recurrence. Of note, 12 of 13 patients with FMR with MR recurrence in our study had LVEDVi ≥ 88 ml/m^2.

Separate linear regression models revealed bivariate associations between all parameters included and VCA at 6-month follow-up (LVEDVi: $\beta = 0.005$ [95% CI, 0.002 to 0.007; $P < .001$]; tenting(vol): $\beta = 0.06$ [95% CI, 0.01 to 0.10; $P = .015$]; tenting index: $\beta = 1.32$ [95% CI, 0.54 to 2.1; $P = .001$]; VCA: $\beta = 0.30$ [95% CI, 0.10 to 0.50; $P = .004$]). The effect of baseline LVEDVi on MR recurrence did not change after including all variables into one multivariate model ($\beta = 0.005$; 95% CI, 0.001 to 0.009; $P = .02$), while all other effects decreased (tenting[vol]: $\beta = -0.07$ [95% CI, −0.14 to 0.01; $P = .10$]; tenting index: $\beta = 0.08$ [95% CI, −0.45 to 2.15; $P = .19$]; and VCA: $\beta = 0.19$ [95% CI, −0.01 to 0.39; $P = .07$]) compared with the previous models fitted separately for each parameter. Using stepwise model selection, only LVEDVi remained as the most relevant determinant. Thus, LVEDVi seems to have the strongest independent influence on outcome. R^2 for LVEDVi was 0.27, meaning that 27% of the variance of VCA was explained by LVEDVi.

DISCUSSION

To the best of our knowledge, this is the first study to comprehensively analyze the association of 3D echocardiographic MV geometry in concert with LV size and function on MR recurrence and MV remodeling after TMVR and the differences between patients with FMR and those with OMR. In all, 34% of patients (21 of 61) had MR recurrence at follow-up, which is in line with the reported 34% of patients (26 of 76) with MR > 2+ at 1 year after TMVR in the EVEREST study,[4] but the rates were higher compared with the ACCESS-EU (A Two-Phase

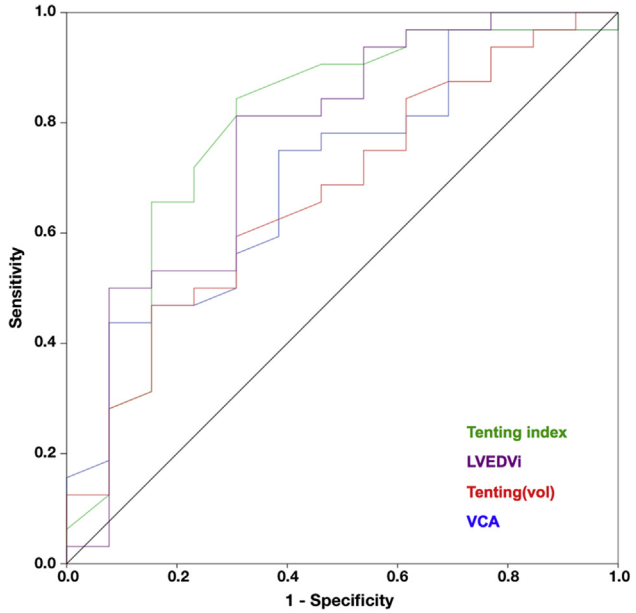

Figure 4 Receiver operating characteristic analysis of parameters associated with MR recurrence. Receiver operating characteristic analysis revealed the largest AUCs for tenting index (0.79; *green line*) and LVEDVi (0.76; *violet line*) as the strength for identifying a cutoff value for the development of MR recurrence. Tenting(vol) (AUC 0.67; *red line*) and VCA (AUC 0.70; *blue line*) showed less strength.

Observational Study of the MitraClip System in Europe) study (21.1% [69 of 327]) and the recent COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) study (22.8% [51 of 222]).[6,28]

In our assessment of the results to understand MR recurrence after TMVR, we found (1) that significantly increased MV tethering at baseline in patients with FMR with MR recurrence, who also had significantly larger values of tenting index, tenting(vol), LVEDVi, and VCA, was associated with poor 6-month outcome, and (2) that there were significant differences in MV geometric remodeling between patients with MR $<$ 0.6 and MR $\geq$ 0.6 as well as between patients with FMR and those with OMR.

Parameters Associated with 6-Month Outcome after TMVR

According to our hypothesis of 3D MV geometric parameters being associated with 6-month outcome before TMVR, we found in patients with FMR that stronger MV tethering with larger tenting index and tenting(vol) in the presence of larger LVEDVi and VCA (Table 3) was associated with recurrent MR at 6-month follow-up, with the multivariate analysis identifying LVEDVi to be the strongest independent determinant of MR recurrence. Although Altiok *et al.*[14] described larger preprocedural annulus(area) in patients in whom TMVR resulted in a VCA reduction of only $\leq$50% as another potential predictor, and Mantegazza *et al.*[19] described a larger preprocedural annulus(AP) ($\geq$4.44 cm) to be predictive of MR reduction of less than two grades at 6-month follow-up, neither could be observed in our study. Furthermore, moderate to severe preprocedural LV dilation was reported to predict progressive LV dilation and MR recurrence after surgical MV repair,[29] but this information for TMVR outcome is rare in 1-year outcome studies.[4-6] Compared with our results for LVEDVi (MR $<$ 0.6 = 68.0 ml/m^2 vs MR $\geq$ 0.6 = 99.9 ml/m^2), Altiok *et al.* and Mantegazza *et al.* described no preprocedural difference in LVEDV and LVEDVi in the two outcome groups (205.2 vs 205.0 ml and 89 vs 93 ml/m^2).

Remodeling of MV Geometry at 6-Month Follow-up after TMVR

We found significant differences in MV geometry remodeling between the MR $<$ 0.6 and MR $\geq$ 0.6 groups and between patients with FMR and those with OMR at follow-up. In patients with FMR, we found an improvement of MV geometry with decreases in LVEDVi and the MV tenting parameters of tenting index and tenting(vol) in the MR $<$ 0.6 group but no reduction of annular size and a moderate increase in MV annular dilation and tenting with an increase of LVEDVi in the MR $\geq$ 0.6 group. Thus, good results in the MR $<$ 0.6 FMR group were less related to reverse remodeling of MV annular dilation but rather to reduced leaflet tethering that resulted from reverse LV remodeling, as indicated by decreased LVEDVi, tenting index, and tenting(vol) (Table 4, Figure 5). Contrary to recent reports of reverse LV remodeling after successful TMVR,[14,17,19,30] we did not find a significant improvement of MV geometry in the MR $<$ 0.6 OMR group. Moreover, we did not observe a significant reduction in the MV annular dimensions of annulus(AP) and annulus(ALPM) at 6-month follow-up in patients with MR $<$ 0.6 in either the FMR or OMR group, which is in contrast to other studies showing reductions in annulus(AP) immediately after TMVR,[15-17,31] at 6-month follow-up,[31] and after 1 year.[32] MV remodeling at 6-month follow-up in the MR $\geq$ 0.6 OMR group was characterized by increases in MV annular diameters annulus(ALPM) and annulus(AP) and increases in annulus(area) and ML(area), most likely as a result of marked worsening of MR in this group, in which prolapse(vol) was much larger already at baseline and also at follow-up compared with the MR $<$ 0.6 OMR group. Thus, a large prolapse(vol) is a potential determinant of difficult or unsuccessful TMVR, but it did not achieve statistical significance, potentially because of the limited study group size. We considered the decrease in LVEDVi observed in patients with OMR with MR $\geq$ 0.6 to be caused by increased transmitral LV ejection toward the low-pressure system under the condition of lowered LV afterload as a result of worsened MR, this pathomechanism being characteristic of acute MR in presence of preserved LV function.[33]

The markedly different characteristics of MV remodeling after TMVR in the two mechanisms of FMR and OMR demonstrated in our study support the understanding of FMR and OMR as two fundamentally different MV diseases, where FMR is the consequence of ventricular or atrial dysfunction and OMR is caused by progressive primary valve disease.[34]

Clinical Implications

Our findings support the concept of a "point of no return" in patients with FMR with advanced LV dilation and severe MV tethering, beyond which TMVR cannot successfully prevent progression of MV dilation and tethering, whereas in patients with less dilated left ventricles this process has not yet been triggered or can be successfully reversed. This may explain the differences in outcomes in the recent MITRA-FR (Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral

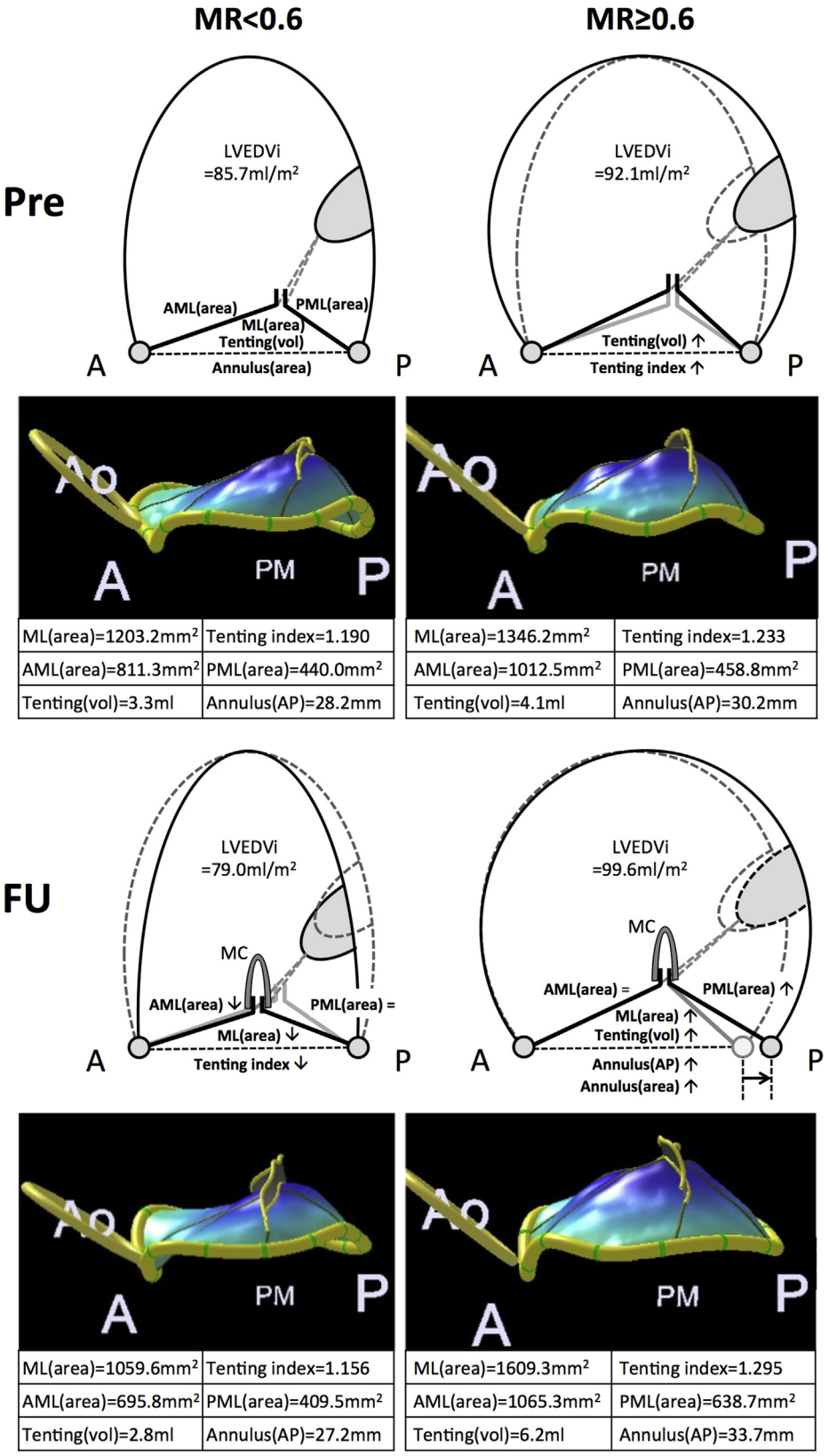

Figure 5 Principle of MV remodeling after MitraClip implantation in patients with FMR. Illustration of MV remodeling after MitraClip implantation in MR < 0.6 versus MR ≥ 0.6 patients with FMR. MR < 0.6 patients showed reductions of LVEDVi and ML tethering at follow-up (FU; *bottom left*) compared with preprocedural state. Decreases in AML(area), ML(area), and tenting index are indicated by *downward arrows*. Patients with MR ≥ 0.6 presenting with larger LVEDVi and MV tethering at baseline *(top right)* compared with MR < 0.6 patients showed increased dimensions of LVEDVi, PML(area), ML(area), annulus(area), and annulus(AP) at follow-up, indicated by *upward arrows (bottom right)*. *A*, Anterior; *Ao*, aorta; *MC*, MitraClip; *P*, posterior; *PM*, posteromedial.

Regurgitation) and COAPT studies (e.g., MITRA-FR patients who had worse clinical outcomes had more advanced LV dilation with larger LVEDVi compared with COAPT study patients).[28,35] Evidence of progressive MV geometric dilation and tethering due to worsening of LV impairment by LV dilation and LV dP/dt lowering in patients with FMR has also been reported to be associated with MR recurrence in prior studies on surgical MV repair.[36,37] As our study results demonstrate that remodeling of MV geometry after TMVR beyond this point of no return is determined not only by leaflet clipping but also by forces external to the mitral apparatus (i.e., LV dilation and consecutive MV dilation and tethering), further studies should investigate whether outcomes in patients with LV dilation and MV tethering beyond this point of no return can be improved by combining TMVR with annuloplasty techniques. Furthermore, our study results imply that progressive MV tethering promoted by advanced LV dilation is the cause of MR recurrence and not the consequence; thus, it is important to better understand the reasons of progressive LV failure with MV tethering in patients with FMR beyond this point of no return. Ongoing LV failure potentially fostered by abnormal intraventricular fluid dynamics in dilated left ventricles with poor ejection fractions has recently been reported to be aggravated after TMVR, potentially promoting long-term adverse LV remodeling.[38]

Limitations

Limitations of our study include its single-center design and the small patient numbers (61 of 133); for example, the small number of patients with OMR may prevent the identification of anatomic determinants of recurrent MR in patients with OMR. As another limitation, the sensitivity and specificity of the LVEDVi cutoff value were not derived from an independent validation population but from the study population from which this value was optimized; thus the accuracies presented represent a "best case" and should be tested in an independent population. However, we reported the AUCs from the study cohort data as being independent of this limitation. All procedures were performed with the first-generation MitraClip system. However, the new MitraClip NTR device has the same size as the first-generation MitraClip system, and therefore effects on MV geometry should be similar. With the recently introduced larger MitraClip XTR device, improved intraprocedural coaptation in severe FMR cases should be obtainable. Another aspect potentially limiting the applicability of our study results to current TMVR therapy is the use of 1.1 clips compared with a mean of 1.5 or 1.7 clips per procedure reported by others,[28,39] thus reflecting a learning curve in the field of TMVR therapy (i.e., larger numbers of implanted clips and less restrictive selection of patients according to the EVEREST criteria).

CONCLUSION

Comprehensive 3D echocardiographic analysis of MV geometry and two-dimensional echocardiographic LV size and function revealed MR recurrence in patients with FMR to be strongly associated with advanced LV dilation and MV tethering at baseline, with LVEDVi being the strongest independent determinant. In patients with OMR, however, no significant determinants of MR recurrence could be identified despite associations with progressive MV annular dilation, leaflet enlargement, and prolapse size. Finally, the study results provide strong clinical evidence for a point of no return in patients with FMR beyond which progressive LV dilation and MV tethering cannot be effectively reversed by TMVR.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.echo.2021.02.017.

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