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NEW RESEARCH PAPER

FOCUS ON MITRAL VALVE REPAIR AND REPLACEMENT

Implications of Mitral Annular Disjunction in Patients Undergoing Transcatheter Edge-to-Edge Repair for Degenerative Mitral Regurgitation

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ABSTRACT

BACKGROUND Little is known about mitral transcatheter edge-to-edge repair (TEER) in patients with mitral annular disjunction (MAD).

OBJECTIVES The authors sought to explore TEER for degenerative mitral regurgitation (MR) according to MAD status.

METHODS We retrospectively analyzed 271 consecutive patients (median age 82 [Q1-Q3: 75-88] years, 60.9% men) undergoing an isolated, first-ever TEER for whom there were viewable preprocedural echocardiograms. Stratified by MAD status at baseline, the cohort was evaluated for all-cause mortality, heart failure hospitalizations, and mitral reinterventions—the composite of which constituted the primary outcome—as well as functional capacity and residual MR, all along the first postprocedural year.

RESULTS Individuals with (n = 62, 22.9%) vs without MAD had more extensive prolapse and larger valve dimensions. Although the former's procedures were longer, utilizing more devices per case, technical success rate and residual MR were comparable. MAD presence was associated with higher mortality risk (HR: 2.64; 95% CI: 1.82-5.52; $P = 0.014$), and increased MAD length—with lower odds of functional class ≤II (OR: 0.65; 95% CI: 0.47-0.88; $P = 0.006$). Among 47 MAD patients with retrievable 1-month data, MAD regressed in 91.5% and by an overall 50% (Q1-Q3: 22%-100%) compared with baseline ($P < 0.001$). A greater MAD shortening conferred attenuated risk for the primary outcome.

CONCLUSIONS In our experience, TEER for degenerative MR accompanied by MAD was feasible and safe; however, its postprocedural course was somewhat less favorable. MAD shortening following TEER was observed in most patients and proved prognostically beneficial. (J Am Coll Cardiol Intv 2023;16:2835-2849) © 2023 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

3D = 3-dimensional

HF = heart failure

LAVi = left atrial volume index

LV = left ventricular

MAD = mitral annular disjunction

MR = mitral regurgitation

MV = mitral valve

MVP = mitral valve prolapse

PVFP = pulmonary venous flow pattern

TEE = transesophageal echocardiography

TEER = transcatheter edge-to-edge repair

TMPG = transmitral mean pressure gradient

TTE = transthoracic echocardiography

Mitral annular disjunction (MAD) is a condition characterized by separation of the mitral annulus from its adjacent myocardial wall, most evident during ventricular systole. Commonly, it is accompanied by exaggerated degenerative changes in the mitral valve (MV). An increasingly recognized entity, MAD has been shown to affect about a third of individuals with mitral valve prolapse (MVP) using various imaging modalities.[1] Among such cases, the presence of MAD has been linked to heightened arrhythmic activity, the correlation of which with long-term survival is still debatable.[2] Despite its high prevalence and association with altered MV geometry, there are currently scarce data regarding the implications of MAD in patients referred for MV interventions, and particularly transcatheter edge-to-edge repair (TEER). Also, it is unknown whether mitral TEER can modify MAD and its related consequences. To address this, we explored the characteristics and outcomes of patients undergoing TEER for MVP-associated MR as a function of MAD presence and extent at baseline, using a large, contemporary sample. Further, we evaluated the change in MAD length following the procedure and assessed whether this change impacts the postprocedural course as well.

METHODS

STUDY POPULATION AND OUTCOMES. Our study represents a retrospective analysis of consecutive adult patients referred for an isolated TEER for above-moderate MR attributed to MVP at Cedars-Sinai Medical Center between January 1, 2013, and January 1, 2021. Patients who had undergone previous mitral procedures and those with no retrievable baseline transthoracic echocardiographic (TTE) images of sufficient quality were excluded.

The primary outcome was the composite of all-cause mortality, heart failure (HF) hospitalizations, or mitral reinterventions at 1-year postprocedure. Secondary outcomes included individual components of the primary outcome, as well as the maintenance of NYHA functional class I to II and residual MR of up to moderate degree at 1 month and 1 year after the intervention.

Conforming to the Declaration of Helsinki, the study was approved by Cedars-Sinai's Institutional Review Board, which waived the requirement for informed consent.

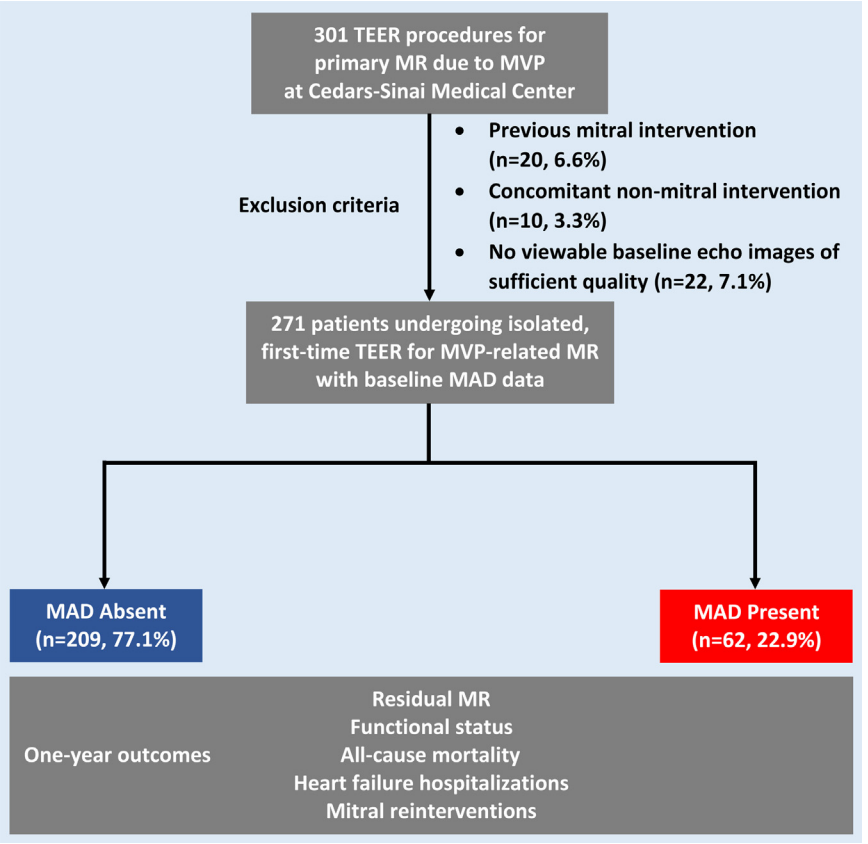
PROCEDURAL ASPECTS. Procedures were decided upon by a heart team that weighed patient preferences and best scientific evidence at the time. All employed the MitraClip system (Abbott Vascular) and were conducted under general anesthesia, utilizing a transseptal approach and a femoral venous access. Transesophageal echocardiography (TEE), fluoroscopy, and right heart catheterization served for guidance and monitoring. Technical success was defined as actual device deployment without the need for subsequent surgical intervention or major complications within the first 24 hours.[3]

ECHOCARDIOGRAPHIC ASSESSMENT. Echocardiograms were performed and interpreted by experienced sonographers and level III-trained echocardiologists, and in accordance with accepted guidelines.[4-6] The ultrasound system used was EPIQ (Philips). Post-processing utilized PICOM365 (SciImage), QLAB 12.0 (Philips), and TomTec Arena (TomTec Imaging Systems) for 2-dimensional (2D), 3-dimensional (3D), and speckle-tracking measurements, respectively.

MR severity was evaluated by integration of qualitative and quantitative measures, whenever feasible. A standardized 5-level grading system was utilized, in which grade 0, 1+, 2+, 3+, or 4+ denoted an up-to-minimal, mild/mild-to-moderate, moderate, moderate-to-severe, or severe regurgitation, respectively. MV annular diameters were assessed at maximal valve opening (ie, mid-diastole). MV area and posterior MV leaflet length were measured using multiplanar reconstruction of 3D images and direct long-axis 2D images, respectively, both obtained from the intraprocedural TEE.

The presence of MVP was ascertained on the intraprocedural TEE as well, upon the demonstration of a ≥2-mm atrial displacement of 1 or more MV leaflets from the MV annular level at end-systole. Also determined according to TEE were prolapse distribution and height and the presence of accompanying flail. Both 2D and 3D images of focused bicommisural, 2-, 3-, and 4-chamber views were utilized for these purposes, with emphasis given to the long-axis view. MAD assessment followed a recent international expert consensus statement.[7] In short, zoomed, long-axis views of baseline and 1-month TTEs were scrutinized, frame-by-frame, for the occurrence of any "trench" in the posterobasal left ventricular (LV) wall, as well as a posterior movement of the posterior MV annular edge to a point seemingly "behind" the LV wall. The extent of MAD was quantified by the length, in mm, of a straight line drawn from the MV annular plane to the most proximal part of the myocardial bulge accompanying the aforementioned findings.

FIGURE 1 Study Flow Chart



MAD = mitral annular disjunction; MR = mitral regurgitation; MVP = mitral valve prolapse; TEER = transcatheter edge-to-edge repair.

Whereas the presence of MAD was determined by dynamic evaluation through the entire cardiac cycle, its degree was dictated by the maximal systolic length.

LV global longitudinal strain was calculated by averaging endocardial strain measurements in the apical 2-, 3-, and 4-chamber windows of the pre-procedural TTE. A semiautomatic approach was used, with manual adjustments of the cardiac cycle duration and traced borders as needed. Both MV dimensions, MAD, and LV global longitudinal strain were retrospectively evaluated by an echocardiologist (A.S.) blinded to patient history. To evaluate inter-observer variability, a second echocardiologist (R.J.S.) examined a random sample of patients as well.

Intraprocedural pulmonary venous flow pattern (PVFP) response following clip deployment was determined by the highest peak systolic to peak diastolic velocity ratio on any pulmonary vein, as measured by a pulsed-wave Doppler beam placed within 1 cm of the pulmonary vein ostia. An improvement in the PVFP was defined by an increase in the ratio from baseline, whereas normalization was defined as a newly appearing ratio of ≥1.

DATA COLLECTION. Patient assessment was carried out at baseline, hospital discharge, and 1 month and 1 year post-TEER. Data regarding clinical parameters were extracted from an electronic medical chart (CS-Link, Epic), which was updated in real time by medical providers and state authorities. For ventricular ectopy (ie, premature ventricular beats, ventricular tachycardia, or ventricular fibrillation), follow-up notes, surface electrocardiograms, and continuous monitoring reports were used as applicable.

STATISTICAL ANALYSIS. The study cohort was first analyzed according to MAD status at baseline.

TABLE 1 Baseline Clinical Characteristics of the Total Cohort

	Total Cohort (N = 271)	MAD Absent (n = 209)	MAD Present (n = 62)	*P* Value
Demographic details				
Age, y	82 (75-88)	82 (75-88)	82 (76-87)	0.925
Male	165 (60.9)	125 (59.8)	40 (64.5)	0.505
Comorbidities				
Body surface area, Mosteller formula, m^2	1.8 (1.6-2.0)	1.8 (1.6-2.0)	1.7 (1.6-2.0)	0.633
Diabetes mellitus	50 (18.6)	40 (19.2)	10 (16.4)	0.616
Hypertension	212 (78.2)	170 (81.3)	52 (83.9)	0.823
Smoking	9 (3.4)	6 (2.9)	3 (5.1)	0.418
Chronic obstructive pulmonary disease	34 (12.5)	22 (10.5)	12 (19.4)	0.065
Anemia	148 (54.6)	114 (54.5)	34 (54.8)	0.968
Stage ≥III chronic kidney disease	199 (74.8)	153 (73.9)	46 (78.0)	0.527
Previous myocardial infarction, PCI, or CABG	74 (27.3)	60 (28.7)	14 (22.6)	0.342
Prior stroke or transient ischemic attack	39 (14.4)	32 (15.3)	7 (11.3)	0.428
Peripheral arterial disease	22 (8.1)	18 (8.6)	4 (6.6)	0.792
Atrial fibrillation/flutter	149 (55.0)	112 (53.6)	37 (59.7)	0.397
Ventricular arrhythmias in the preceding year				0.646
Total	17 (6.3)	13 (6.2)	4 (6.5)	
Ventricular premature beats	4 (1.5)	4 (1.9)	0 (0.0)	
Nonsustained ventricular tachycardia	10 (3.7)	7 (3.3)	3 (4.8)	
Sustained ventricular tachycardia / ventricular fibrillation	3 (1.1)	2 (1.0)	1 (1.6)	
Intraventricular conduction delay, QRS duration ≥120 ms				
Total	47 (18.2)	41 (20.6)	6 (10.0)	0.102
Complete left bundle branch block	8 (3.1)	7 (3.5)	1 (1.7)	0.686
Non-complete left bundle branch block	39 (15.1)	34 (17.1)	5 (8.3)	0.097
Heart failure features				
NYHA functional class				0.865
II	22 (8.1)	16 (7.7)	6 (9.7)	
III	122 (45.0)	94 (45.0)	28 (45.2)	
IV	127 (46.9)	99 (47.4)	28 (45.2)	
KCCQ12 score, points	46.88 (23.96-69.79)	43.75 (22.92-65.10)	55.21 (29.95-78.78)	0.058
6-Minute walk test distance, m	274 (152-366)	259 (152-366)	274 (151-366)	0.687
Serum B-type natriuretic peptide level, pg/mL	305 (156-567)	320 (181-560)	237 (110-612)	0.220
Procedural risk				
Society of Thoracic Surgeons score for mitral valve repair, points	4.7 (2.6-7.4)	4.8 (2.8-7.9)	4.5 (2.3-6.5)	0.187
Mitral Regurgitation International Database score, points	9 (7-10)	9 (7-10)	8 (7-10)	0.133
MitraScore, points	3 (2-4)	3 (2-4)	3 (2-4)	0.287
Treatment				
Medications				
Beta-blockers	159 (58.7)	128 (61.2)	31 (50.0)	0.114
Renin angiotensin system inhibitors	125 (46.1)	98 (46.9)	27 (43.5)	0.643
Mineralocorticoid receptor antagonists	29 (10.7)	26 (12.4)	3 (4.8)	0.089
Loop diuretic agents	167 (61.6)	130 (62.2)	37 (59.7)	0.720
Antiarrhythmic agents	48 (17.8)	38 (18.3)	10 (16.1)	0.699
Antiplatelet agents	154 (56.8)	118 (56.5)	36 (58.1)	0.823
Oral anticoagulants	118 (43.5)	93 (44.5)	25 (40.3)	0.560
Cardiac implantable electronic device				
Total	43 (15.9)	32 (15.3)	11 (17.7)	0.645
Pacemaker	36 (13.3)	28 (13.4)	8 (12.9)	0.920
Implantable cardioverter defibrillator	3 (1.1)	2 (1.0)	1 (1.6)	0.543
Cardiac resynchronization therapy	2 (0.7)	1 (0.5)	1 (1.6)	0.406
Cardiac resynchronization therapy-defibrillator	2 (0.7)	1 (0.5)	1 (1.6)	0.406
Hemodialysis	6 (2.2)	6 (2.9)	0 (0.0)	0.343

Values are median (Q1-Q3) or n (%).

CABG = coronary artery bypass grafting; KCCQ = Kansas City Cardiomyopathy Questionnaire; MAD = mitral annular disjunction; PCI = percutaneous coronary intervention.

Subsequent analyses were performed in the subgroup of patients who had both MAD preprocedurally and a viewable echocardiogram allowing for MAD assessment at 1 month following TEER.

Variables were reported as frequency (percentage) or median (IQR). Intergroup differences were evaluated using Pearson's chi-square, Fisher exact, or Mann-Whitney *U* tests. Change over time in the same parameters was assessed by McNemar or Wilcoxon

TABLE 2 Baseline Echocardiographic Data of the Total Cohort

	Total Cohort (N = 271)	MAD Absent (n = 209)	MAD Present (n = 62)	*P* Value
Baseline echocardiogram time before TEER, d	29 (9–56)	29 (11–54)	30 (8–65)	0.814
Mitral valve parameters				
Mitral regurgitation severity				0.508
Moderate-to-severe	45 (16.6)	33 (15.8)	12 (19.4)	
Severe	226 (83.4)	176 (84.2)	50 (80.6)	
Mitral effective regurgitant orifice area by PISA, cm^2	0.40 (0.28–0.52)	0.39 (0.28–0.51)	0.43 (0.31–0.58)	0.177
Mitral regurgitant volume by PISA, mL	55.9 (42.5–76.2)	53.8 (40.9–75.2)	62.6 (51.3–81.6)	0.142
Transmitral mean pressure gradient, mm Hg	3 (2–4)	3 (2–4)	2 (2–4)	**0.040**
Mitral valve area, cm^2	5.1 (4.2–6.4)	5.0 (4.0–6.4)	5.8 (4.9–6.8)	0.059
Degenerative disease characteristics				
Mitral annular diameter, mm				
Anterior-posterior	29.1 (25.6–33.0)	29.0 (25.4–32.6)	30.0 (25.7–34.0)	0.321
Medial-lateral	32.7 (29.1–36.2)	32.2 (28.8–35.9)	33.8 (30.4–36.7)	0.089
Posterior leaflet length, mm	16.0 (12.0–20.0)	15.0 (11.0–19.0)	19.0 (16.0–22.0)	**<0.001**
Prolapse distribution				**0.005**
Anterior leaflet only	47 (17.3)	44 (21.1)	3 (4.8)	
Posterior leaflet only	163 (60.1)	124 (59.3)	39 (62.9)	
Both leaflets	61 (22.5)	41 (19.6)	20 (32.3)	
Scallops	1 (1–2)	1 (1–2)	1 (1–2)	0.283
Prolapse height, mm	6.0 (5.0–8.0)	6.0 (5.0–8.0)	8.0 (6.0–9.0)	**0.003**
Accompanying flail	114 (42.1)	86 (41.1)	28 (45.2)	0.674
Mitral annular disjunction-related findings				
Lateral s' velocity				
Median, cm/s	9.0 (8.0–11.0)	9.0 (7.0–10.5)	10.5 (8.0–13.0)	**<0.001**
≥16 cm/s, Pickelhaube sign	7 (2.6)	3 (1.4)	4 (6.5)	**0.029**
Above-mild mitral annular calcification	34 (12.5)	29 (13.9)	5 (8.1)	0.225
Left heart parameters				
Left ventricular ejection fraction, %	63 (56–68)	63 (56–68)	62 (56–68)	0.717
Left ventricular end-diastolic diameter, cm	4.9 (4.5–5.4)	4.9 (4.5–5.5)	4.9 (4.4–5.3)	0.469
Index, cm/m^2	2.8 (2.5–3.1)	2.8 (2.5–3.1)	2.7 (2.5–3.1)	0.648
Left ventricular end-systolic diameter, cm	3.2 (2.7–3.6)	3.3 (2.7–3.7)	3.0 (2.8–3.3)	0.127
Index, cm/m^2	1.8 (1.5–2.1)	1.8 (1.5–2.1)	1.7 (1.5–2.0)	0.167
Left ventricular mass index, ASE formula, g/m^2	119.1 (93.1–140.5)	120.7 (96.4–141.7)	111.8 (85.6–129.4)	**0.024**
Left atrial diameter, cm	5.2 (4.6–6.6)	5.3 (4.7–6.8)	4.8 (3.9–5.9)	**0.038**
Left atrial volume index, mL/m^2	59.2 (44.0–78.0)	62.0 (45.3–77.0)	52.3 (39.0–79.0)	**0.026**
Moderate and above aortic stenosis/regurgitation	18 (6.6)	14 (6.7)	4 (6.5)	1.000
Right heart parameters				
Qualitative right ventricular dysfunction	59 (24.3)	43 (23.4)	16 (27.1)	0.559
Right ventricular end-diastolic basal diameter, cm	3.9 (3.4–4.3)	3.9 (3.4–4.3)	4.0 (3.5–4.5)	0.204
Above-moderate tricuspid regurgitation	44 (16.4)	35 (16.9)	9 (14.5)	0.655
TAPSE, mm	18 (15–22)	18 (15–23)	18 (16–22)	0.801
PASP, mm Hg	43 (32–56)	43 (32–56)	41 (34–54)	0.995
TAPSE/PASP, mm/mm Hg	0.44 (0.30–0.62)	0.41 (0.30–0.62)	0.51 (0.31–0.69)	0.341
Speckle tracking				
Longitudinal strain, %				
Global	−15.9 (−19.3 to −12.4)	−15.4 (−19.1 to −12.0)	−17.3 (−19.7 to −14.6)	0.174
Posterobasal	−17.3 (−24.0 to −9.6)	−17.1 (−23.5 to −9.6)	−20.4 (−27.1 to −9.4)	0.305
Inferobasal	−11.0 (−16.4 to −6.0)	−11.1 (−16.4 to −5.4)	−10.7 (−16.4 to −6.8)	0.860

Values are median (Q1-Q3) or n (%). Figures in **bold** denote statistical significance.

ASE = American Society of Echocardiography; MAD = mitral annular disjunction; PASP = pulmonary arterial systolic pressure; PISA = proximal isovelocity surface area; TAPSE = tricuspid annular plane systolic excursion; TEER = transcatheter edge-to-edge repair.

tests. Correlation between continuous variables was estimated by the Pearsons' *r* coefficient. Interobserver reliability was determined using the intraclass correlation coefficient.

The probabilities of experiencing the primary outcome as a function of MAD presence at baseline and of the change in MAD length from baseline to 1-month post-procedure were graphically displayed according to the Kaplan-Meier method, with comparisons of cumulative event-free survival rates using the log-rank test. Independent associations involving either baseline MAD status or the change in MAD length following TEER were determined by Cox or binary logistic regression multivariable analyses, as

TABLE 3 Procedural Details and Periprocedural Course in the Total Cohort

	Total Cohort (N = 271)	MAD Absent (n = 209)	MAD Present (n = 62)	*P* Value
Presentation				
Acute decompensated heart failure	19 (7.0)	17 (8.1)	2 (3.2)	0.260
Cardiogenic shock or hemodynamic support	3 (1.1)	3 (1.4)	0 (0.0)	0.343
General procedural aspects				
Urgent procedure	21 (7.7)	16 (7.7)	5 (8.1)	1.000
Total duration, min	109 (87 to 149)	107 (86 to 146)	115 (98 to 159)	**0.036**
Fluoroscopy duration, min	19 (14 to 27)	19 (13 to 26)	22 (15 to 33)	**0.024**
Concomitant atrial septal defect closure	8 (3.0)	5 (2.4)	3 (4.8)	0.389
Complications[a]	6 (2.2)	5 (2.4)	1 (1.6)	0.714
Conversion to surgery	1 (0.4)	1 (0.5)	0 (0.0)	0.585
Device parameters				
Clips deployed				
0, aborted/not deployed	7 (2.6)	7 (3.3)	0 (0.0)	0.357
1	120 (44.3)	97 (46.4)	23 (37.1)	0.195
2	109 (40.2)	82 (39.2)	27 (43.5)	0.543
≥3	35 (12.9)	23 (11.0)	12 (19.4)	0.085
Median	2 (1 to 2)	2 (1 to 2)	2 (1 to 3)	**0.028**
Device generation				
1st	104 (38.4)	83 (29.7)	21 (33.9)	0.406
2nd	77 (28.4)	56 (26.8)	21 (33.9)	0.278
3rd	57 (21.0)	48 (23.0)	9 (14.5)	0.152
4th	33 (12.2)	22 (10.5)	11 (17.7)	0.127
Clip site				
A2P2	256 (94.5)	197 (94.3)	59 (95.2)	0.785
Non-A2P2	29 (10.7)	22 (10.5)	7 (11.3)	0.818
Immediate results				
Right heart catheterization				
V-wave, mm Hg				
Pre-clip deployment	26 (17 to 41)	27 (18 to 43)	23 (15 to 36)	0.051
Post-clip deployment	18 (13 to 24)	18 (13 to 24)	16 (12 to 23)	0.169
Change from pre to post; *P* value for pre vs post	−7 (−17 to −1); **<0.001**	−7 (−19 to −2); **<0.001**	−6 (−15 to −1); **<0.001**	0.288
Mean left atrial pressure, mm Hg				
Pre-clip deployment	16 (12 to 22)	17 (12 to 23)	14 (10 to 19)	**0.004**
Post-clip deployment	13 (10 to 17)	13 (10 to 17)	13 (9 to 16)	0.120
Change from pre to post; *P* value for pre vs post	−2 (−7 to 1); **<0.001**	−3 (−8 to 1); **<0.001**	−1 (−6 to 1); **0.004**	0.116
Mean pulmonary arterial pressure, mm Hg				
Pre-clip deployment	28 (20 to 36)	29 (21 to 38)	23 (20 to 31)	**0.015**
Post-clip deployment	25 (20 to 32)	26 (21 to 34)	23 (19 to 30)	0.106
Change from pre to post; *P* value for pre vs post	−1 (−6 to 3); **0.033**	−1 (−8 to 2); **0.006**	−1 (−4 to 5); **0.011**	0.134
Echocardiography				
Pulmonary venous flow pattern				
Improvement	191 (83.8)	144 (81.8)	47 (90.4)	0.141
Normalization	176 (74.3)	133 (75.6)	43 (76.8)	0.621
Mitral regurgitation severity up-to-mild	207 (76.4)	158 (75.6)	49 (79.0)	0.576
Periprocedural course				
Hospitalization length, d	1 (1 to 1)	1 (1 to 1)	1 (1 to 2)	0.598
In-hospital mortality	2 (0.7)	2 (1.0)	0 (0.0)	0.439
Discharge home	258 (95.9)	199 (96.1)	59 (95.2)	0.720
Medications at 1 month				
Beta-blockers	127 (57.5)	102 (60.0)	25 (49.0)	0.164
Renin angiotensin system inhibitors	108 (49.1)	82 (48.5)	26 (51.0)	0.758
Mineralocorticoid receptor antagonists	23 (10.4)	21 (12.4)	2 (3.9)	0.084
Loop diuretic agents	127 (57.5)	101 (59.4)	26 (51.0)	0.285
Antiarrhythmic agents	43 (19.5)	34 (20.1)	9 (17.6)	0.696
Antiplatelet agents	155 (70.1)	120 (70.6)	35 (68.6)	0.788
Oral anticoagulants	97 (43.9)	77 (45.3)	20 (39.2)	0.443

Values are n (%) or median (Q1-Q3). Figures in **bold** denote statistical significance. [a]Complications were defined as any of the following: thrombotic or bleeding event, cardiac tamponade, leaflet injury, new arrhythmic phenomena (including conduction anomalies), or esophageal tear.

MAD = mitral annular disjunction.

TABLE 4 Echocardiographic Results in the Total Cohort

	Total Cohort (N = 271)	MAD Absent (n = 209)	MAD Present (n = 62)	*P* Value
Follow-up echocardiogram time after TEER, d				
At 1 mo	32 (29-35)	33 (29-35)	31 (29-34)	0.302
At 1 y	371 (361-405)	371 (361-406)	369 (359-403)	0.749
Mitral regurgitation severity at 1 mo				
Up-to-mild	134 (65.7)	105 (67.3)	29 (60.4)	0.379
Change from baseline, grades	−3 (−3 to [−2])	−3 (−3 to [−2])	−3 (−3 to [−2])	0.424
Transmitral mean pressure gradient, mm Hg				
At 1 mo	4 (3-5)	4 (3-5)	3 (3-5)	0.185
At 1 y	4 (3-5)	4 (3-5)	3 (2-4)	0.235
Left ventricular ejection fraction, %				
At 1 mo	58 (52-64)	58 (50-64)	60 (54-62)	0.949
At 1 y	58 (55-65)	58 (53-65)	58 (56-65)	0.439
Left ventricular end-systolic diameter, cm				
At 1 mo	3.2 (2.8-3.7)	3.2 (2.8-3.8)	3.2 (2.7-3.6)	0.239
At 1 y	3.1 (2.7-3.5)	3.1 (2.7-3.4)	3.2 (2.8-3.6)	0.490
Left atrial volume index, mL/m^2				
At 1 mo	52.0 (40.0-73.0)	54.0 (37.3-77.0)	45.5 (35.5-64.0)	**0.011**
At 1 y	53.5 (36.0-71.3)	54.0 (37.3-77.0)	43.0 (26.8-62.0)	**0.022**
Change from baseline to 1 y	−7.0 (−31.2 to 11.3)	−8.0 (−32.1 to 14.0)	−6.4 (−27.8 to 13.2)	0.763
Above-moderate tricuspid regurgitation				
At 1 mo	21 (10.6)	14 (9.3)	7 (14.9)	0.284
At 1 y	7 (6.0)	7 (7.4)	0 (0.0)	0.344
Tricuspid annular plane systolic excursion, mm				
At 1 mo	19 (15-21)	19 (16-22)	19 (15-24)	0.579
At 1 y	18 (15-21)	17 (14-20)	21 (18-25)	**0.010**
Pulmonary arterial systolic pressure, mm Hg				
At 1 mo	37 (29-49)	37 (30-48)	37 (26-50)	0.932
At 1 y	32 (25-43)	32 (26-44)	28 (24-47)	0.465
Mitral annular disjunction length at 1 mo			n = 47	
Median, mm			4.0 (0.0-7.0)	
Change from baseline to 1 mo				
Absolute, mm			−4.0 (−7.0 to −2.0)	
Relative, %			−50.0 (−100.0 to −22.2)	
Trend				
Reduced			43 (91.5)	
Disappeared			17 (36.2)	
Unchanged			2 (4.3)	
Increased			2 (4.3)	
P value for baseline vs 1 mo			**<0.001**	
Lateral s' velocity at 1 mo			n = 36	
Median, cm/s			9.5 (7.0-12.0)	
P value for baseline vs 1 mo			0.090	
≥16 cm/s, Pickelhaube sign			1 (2.1)	

Values are median (Q1-Q3) or n (%). Figures in **bold** denote statistical significance.
Abbreviations as in Table 2.

appropriate. These incorporated preprocedural clinical parameters as well as baseline and 1-month echocardiographic parameters of perceived or previously proven[8] prognostic significance which also possessed a *P* value of <0.10 on univariable models. Acknowledging the possibility of unmeasured bias upon the simultaneous consideration of clinical and echocardiographic variables, and of parameters that were acquired at different time points, both clinical/1-month inclusive and exclusive models were utilized. For the prediction of 1-month MAD decrease equal or greater than the cohort's median, procedural aspects were also included. Collinearity was estimated by the variance inflation factor.

Cases with missing values were censored from the relevant calculations, and a 2-sided *P* value of <0.05 defined statistical significance. SPSS 24 (IBM Corporation) was used for all analyses.

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TABLE 5 Clinical Outcomes in the Total Cohort

	Frequency				Risk Associated With MAD Presence at Baseline		Risk Associated With MAD Length at Baseline	
	Total Cohort (N = 271)	MAD Absent (n = 209)	MAD Present (n = 62)	*P* Value	HR/OR (95% CI)[a]	*P* Value	HR/OR (95% CI)[a]	*P* Value
Primary outcome								
All-cause mortality, heart failure hospitalizations, or mitral reinterventions at 1 y	54 (19.9)	39 (18.7)	15 (24.2)	0.338	1.42 (0.78-2.58)	0.246	1.04 (0.97-1.11)	0.252
Secondary outcomes								
All-cause mortality or heart failure hospitalizations at 1 y	39 (14.4)	28 (13.4)	11 (17.7)	0.392	1.43 (0.71-2.87)	0.318	1.04 (0.96-1.13)	0.360
All-cause mortality at 1 y	23 (8.5)	15 (7.2)	8 (12.9)	0.155	2.64 (1.82-5.52)[b]	**0.014**	1.05 (0.98-1.13)	0.180
Heart failure hospitalizations at 1 y	21 (7.7)	16 (7.7)	5 (8.1)	0.916	1.31 (0.41-3.09)	0.810	1.03 (0.92-1.15)	0.625
Mitral reinterventions at 1 y	20 (7.4)	13 (6.2)	7 (11.3)	0.177	2.02 (0.81-5.07)	0.134	1.09 (0.98-1.20)	0.107
NYHA functional class ≤II and mitral regurgitation severity up-to-moderate								
At 1 mo	165 (82.5)	127 (82.5)	38 (82.6)	0.982	1.00 (0.42-2.41)	0.982	1.00 (0.91-1.12)	0.886
At 1 y	93 (80.2)	76 (81.7)	17 (73.9)	0.394	0.63 (0.22-1.85)	0.403	0.93 (0.82-1.05)	0.231
NYHA functional class ≤II								
At 1 mo	187 (89.5)	144 (88.9)	43 (91.5)	0.789	0.74 (0.24-2.32)	0.610	0.95 (0.83-1.10)	0.493
At 1 y	125 (91.2)	101 (92.7)	24 (85.7)	0.266	0.48 (0.13-1.71)	0.255	0.65 (0.47-0.88)[b]	**0.006**
Mitral regurgitation severity up-to-moderate								
At 1 mo	187 (91.7)	144 (92.3)	43 (89.6)	0.556	0.72 (0.24-2.15)	0.552	0.97 (0.85-1.10)	0.647
At 1 y	105 (89.0)	85 (89.5)	20 (87.0)	0.716	0.78 (0.20-3.12)	0.730	0.96 (0.82-1.12)	0.609
Data availability in alive patients remaining in follow-up								
NYHA functional class and mitral regurgitation severity								
At 1 mo	200/265 (75.5)	154/204 (75.5)	46/61 (75.4)	0.932	0.97 (0.51-1.84)	0.932	1.00 (0.93-1.08)	0.991
At 1 y	116/248 (46.8)	93/194 (47.9)	23/54 (42.6)	0.502	0.80 (0.42-1.54)	0.502	0.97 (0.90-1.05)	0.419
NYHA functional class								
At 1 mo	209/265 (78.9)	162/204 (79.4)	47/61 (77.0)	0.779	0.91 (0.47-1.77)	0.779	1.01 (0.93-1.09)	0.881
At 1 y	137/248 (55.2)	109/194 (56.2)	28/54 (51.9)	0.334	0.76 (0.43-1.34)	0.334	0.96 (0.90-1.03)	0.276
Mitral regurgitation severity								
At 1 mo	204/265 (77.0)	156/204 (76.5)	48/61 (78.7)	0.580	1.22 (0.61-2.42)	0.580	1.04 (0.96-1.13)	0.363
At 1 y	118/248 (47.6)	95/194 (49.0)	23/54 (42.6)	0.425	0.78 (0.43-1.44)	0.426	0.97 (0.91-1.04)	0.434

Values are n (%) or n/N (%) except as noted. Figures in **bold** denote statistical significance in the multivariable models. [a]Per univariable analysis unless specified otherwise. [b]Per multivariable analysis.
MAD = mitral annular disjunction; NA = not applicable.

RESULTS

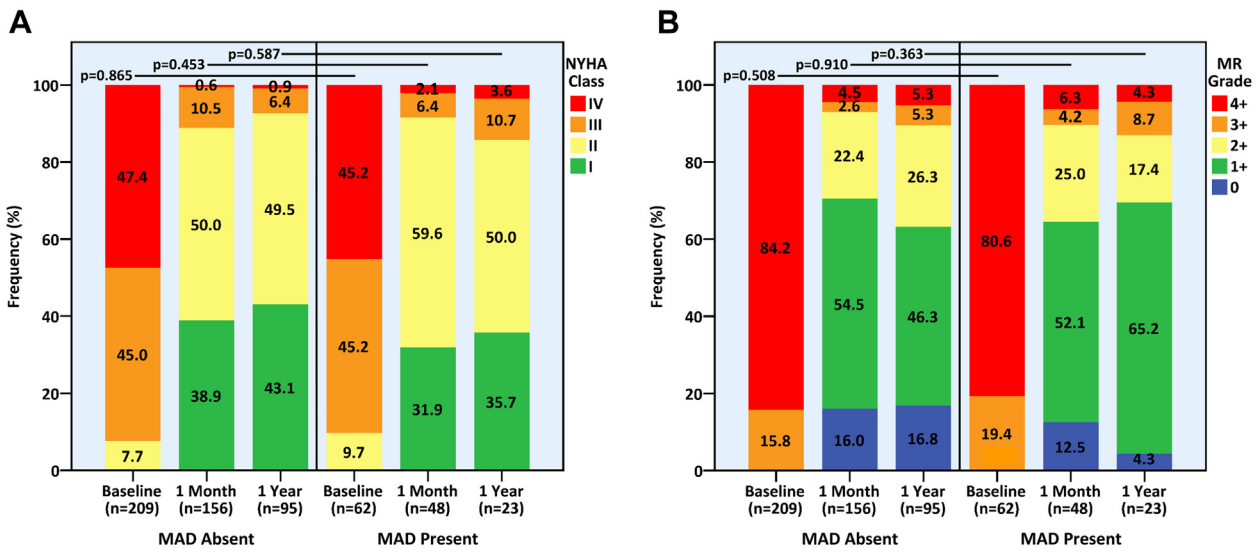
BASELINE CHARACTERISTICS OF THE STUDY POPULATION. A total of 271 patients met inclusion criteria and were followed for 457 (Q1-Q3: 155-992) days (Figure 1). Of them, 62 (22.9%) presented to TEER with MAD, which was similarly distributed in the 2 sexes (n = 40/165, 24.2% among males and n = 22/106, 20.8% among females; $P = 0.505$) and which measured 8.0 (Q1-Q3: 6.0-9.0) mm in length.

Overall, no major differences in clinical characteristics were observed at baseline between the MAD and no-MAD groups (Table 1). Notably, both exhibited an elderly age, a male predominance, a high burden of comorbidities, and a highly symptomatic HF, translating to a medium-to-high surgical and percutaneous risk. A similar proportion of the 2 study groups (~6%) demonstrated ventricular arrhythmias within 1 year preceding TEER, which mostly consisted of nonsustained ventricular tachycardias.

Preprocedural echocardiograms, obtained 29 (Q1-Q3: 9-56) days before TEER, also were generally comparable in those with and without MAD (Table 2). However, the former were more likely to demonstrate a posterior/bileaflet MVP. Also, they had greater prolapse height and MV area, a nonsignificantly larger mitral annular diameter, a longer posterior MV leaflet, and a lower transmitral mean pressure gradient (TMPG). Finally, MAD patients harbored smaller LV mass index, left atrial diameter, and left atrial volume index (LAVi). Of note, the intraclass correlation coefficient proved universally high (>0.80).

PROCEDURAL DETAILS AND PERIPROCEDURAL COURSE. Patients with MAD underwent longer interventions that utilized more devices per case (Table 3). Yet, a significant post-clipping decline in MR to mild or less, achievement of PVFP improvement/normalization, and a high technical success rate were noted irrespective of the presence of MAD.

FIGURE 2 Functional Status and MR Grade Along the First Postprocedural Year in the Total Cohort



(A) Functional status. (B) Mitral regurgitation grade. Abbreviations as in Figure 1.

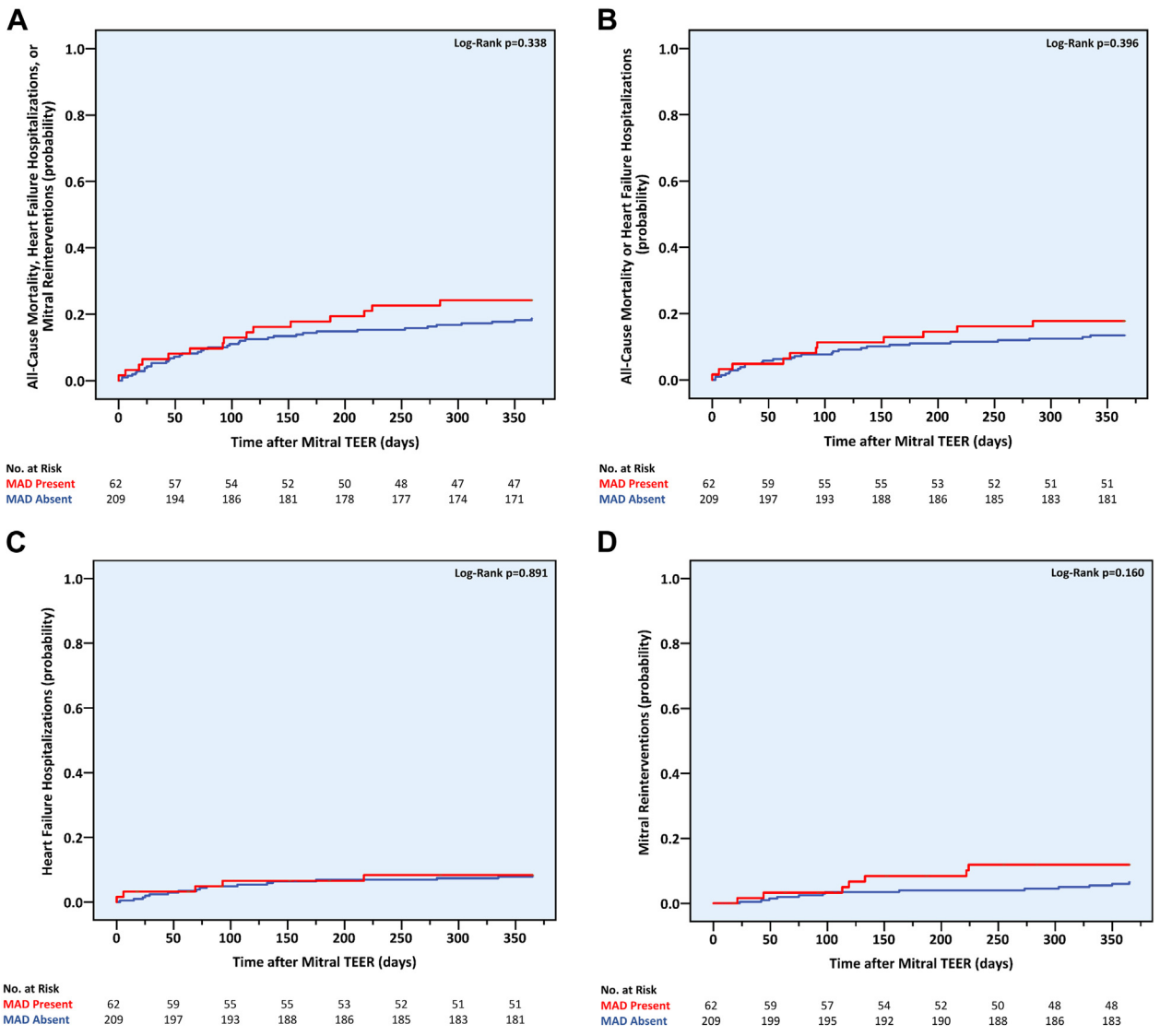
ECHOCARDIOGRAPHIC RESULTS. Both 1-month and 1-year postprocedural echocardiographic findings were largely nondifferent in patients with and without MAD (Table 4). Importantly, MR grade, as a continuous variable, did not correlate with baseline TMPG, the number of deployed clips, or procedural duration, notwithstanding their differences between the 2 study groups. Although LAVi significantly decreased in the MAD group, the change in LAVi from baseline was comparable to that in the no-MAD group.

CLINICAL OUTCOMES. By 1 year after TEER, 54 patients (19.9%) experienced the primary outcome, a composite of all-cause mortality (n = 23, 8.5%), HF hospitalizations (n = 21, 7.7%), or mitral reinterventions (n = 20, 7.4%) (Table 5). Concurrently, both NYHA functional status and MR severity were significantly improved compared with baseline (all $P < 0.001$) (Figure 2) such that 125 (91.2%), 105 (89.0%), and 93 (80.2%) patients who remained alive and had available data maintained a NYHA functional class ≤II, an up-to-moderate MR, and the combination of both, respectively (Table 5).

No significant differences were noted between patients with and without MAD in relation to the rates and cumulative incidences of any of the outcomes explored (Table 5, Figure 3, Supplemental Figure 1). However, the former did exhibit a tendency toward higher mortality (n = 8, 12.9% vs n = 15, 7.2%; $P = 0.155$), which was primarily accounted for by deaths of unknown origin (n = 6, 9.7% vs n = 8, 3.8%; $P = 0.056$), as well as toward shorter survival time (316 ± 13 days vs 347 ± 5 days; log-rank $P = 0.126$). Per multivariable analyses, the presence of MAD was independently associated with a higher mortality risk (HR: 2.64; 95% CI: 1.82-5.52; $P = 0.014$), and an increased MAD length independently conferred lower odds of maintaining NYHA functional class ≤II (OR: 0.65; 95% CI: 0.47-0.88; $P = 0.006$) (Table 5, Supplemental Tables 1 and 2). Importantly, univariable analysis did not demonstrate an association between the number of deployed clips (as a continuous variable) and mortality (HR: 1.48; 95% CI: 0.95-2.10 $P = 0.188$) or NYHA functional class ≤II (OR: 0.71; 95% CI: 0.28-1.82; $P = 0.475$).

SUBGROUP ANALYSIS. Among the 47 MAD patients with available 1-month data, MAD significantly decreased from baseline by 4.0 (Q1-Q3: 2.0-7.0) mm, representing a relative 50.0% (Q1-Q3: 22.2%-100.0%) decline ($P < 0.001$) (Table 4, Figure 4). In absolute terms, a net reduction in MAD length at 1-month postprocedure was observed in 43 (91.5%) of these patients, and a complete regression in 17 (36.2%). At the 1-year mark, all 22 patients (100.0%) still alive and in active surveillance at our institution demonstrated a decrease in MAD length compared with baseline, and one-half (n = 11) had a continued decrease relative to 1 month.

FIGURE 3 1-Year Cumulative Incidence of Clinical Events in the Total Cohort

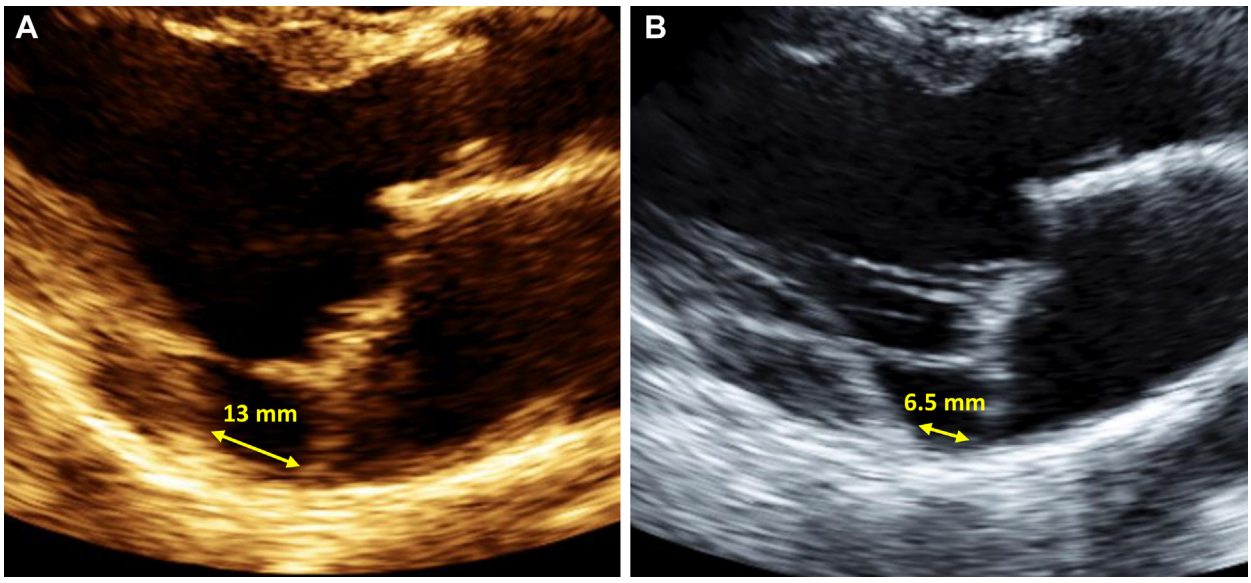


(A) All-cause mortality, heart failure hospitalizations, or mitral reinterventions. (B) All-cause mortality or heart failure hospitalizations. (C) Heart failure hospitalizations. (D) Mitral reinterventions. Abbreviations as in **Figure 1**.

Interestingly, patients showing an equal to or greater than median (ie, ≥50%) decrease in MAD length from baseline to 1 month sustained a lower cumulative incidence of the primary outcome compared with patients with a less-than-median decline (log-rank $P = 0.046$) (Supplemental Figure 2). Furthermore, and according to multivariable analyses, both a ≥50% decrease and a more profound decrease in the 1-month MAD length were independently associated with a reduced risk for the primary outcome (≥50% decrease HR: 0.16; 95% CI: 0.03-0.85; $P = 0.032$; any additional 1-mm decrease HR: 0.75; 95% CI: 0.61-0.92; $P = 0.005$) (Supplemental Tables 3 and 4).

Comparing patients with and without a ≥50% decrease in MAD length from baseline to 1 month, the former exhibited at 1 month a higher LV ejection fraction (60% [Q1-Q3: 55%-64%) vs 57% [Q1-Q3: 49%-60%]; $P = 0.029$) and numerically lower LV end-systolic diameter (3.0 [Q1-Q3: 2.7-3.2] cm vs 3.3 [Q1-Q3: 2.8-3.7] cm; $P = 0.127$) and higher tricuspid annular plane systolic excursion (20 [Q1-Q3: 17-26]

FIGURE 4 MAD Length at Baseline and at 1-Month Postprocedure



(A) Baseline. (B) 1-month post-procedure. MAD = mitral annular disjunction.

mm vs 17 [Q1-Q3: 13-22] mm; $P = 0.076$). Otherwise, no significant differences were noted between the 2 subgroups in relation to pre-, intra-, and post-procedural findings, including baseline MAD length (8.0 [Q1-Q3: 7.0-9.0] mm vs 8.0 [Q1-Q3: 6.0-10.0] mm; $P = 0.499$). Lastly, no baseline echocardiographic parameter or procedural aspect demonstrated a statistically significant association with the extent of MAD regression (Supplemental Table 5).

DISCUSSION

Our study explored the prevalence, correlates, and implications of MAD, as assessed by 2D TTE, in real-world patients referred to TEER for significant degenerative MR. Its main findings, summarized in the **Central Illustration**, are as follows: 1) MAD was observed at baseline in approximately one-fifth of cases, in whom its median length was 8 mm; 2) the presence of MAD was associated with advanced degenerative changes, including more diffuse prolapse and larger prolapse height and MV dimensions; 3) patients with MAD required lengthier interventions and more devices per procedure but nevertheless experienced a similarly high technical success rate; 4) at 1-month postprocedure, MAD regressed in >90% of patients with available data and by an overall 50% compared with baseline; and 5) MAD status at baseline and its change following TEER were not predictive of residual MR; however, MAD existence was associated with increased risk for death, a more prominent MAD conferred higher odds of functional disability persistence, and a decline in MAD length at 1 month compared with baseline was associated with reduced risk for the primary composite outcome of all-cause mortality, HF hospitalizations, or mitral reinterventions.

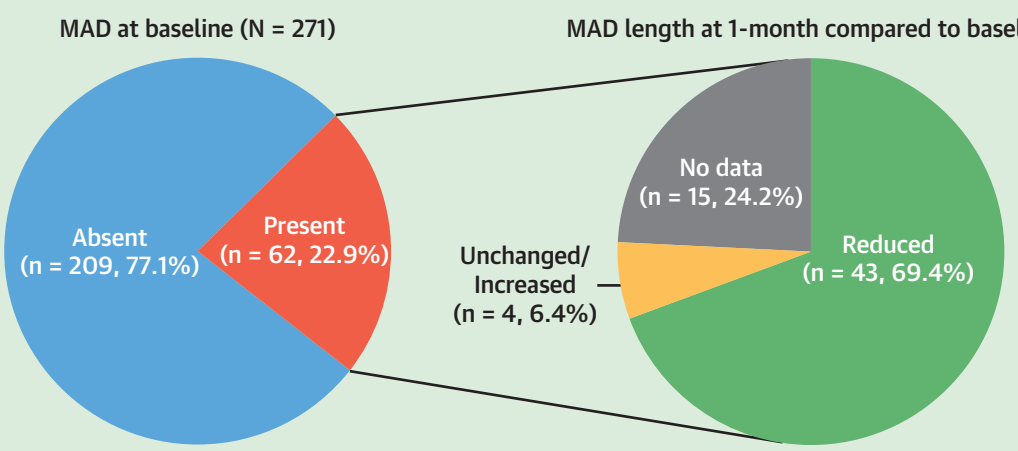
The study's observations suggest MAD as a rather prevalent condition in the mitral TEER population, thus resembling studies performed in patients with significant MR not subjected to TEER.[9,10] Considering that no patient at our institution received the diagnosis in real time, the study also highlights MAD as an under-reported phenomenon in this subset of patients, constituting an easily correctable awareness gap. Whether the combination of MAD and significant MR necessitating intervention is truly more prevalent among males, as might be suspected based on our and others' findings,[11,12] or whether our results merely represent a referral/selection bias (possibly encountered in prior publications dominated by males as well) is an intriguing question for future prospective research.

Another notion arising from our study relates to the potential role of MAD in marking valvular and, consequently, procedural complexity in patients

CENTRAL ILLUSTRATION **Implications of Mitral Annular Disjunction in Transcatheter Edge-to-Edge Repair**

MitraClip and Mitral Annular Disjunction (MAD)

A Prevalence



B MAD Correlates

Preprocedure

- Overall comparable clinical and echocardiographic characteristics
- More extensive degenerative changes
- Greater mitral valve area and marginally larger annulus

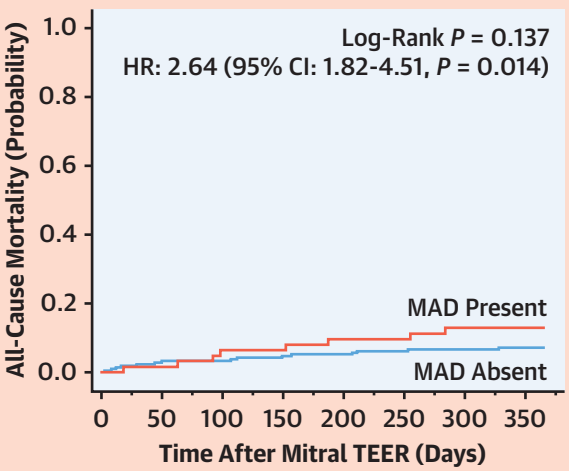
Procedure

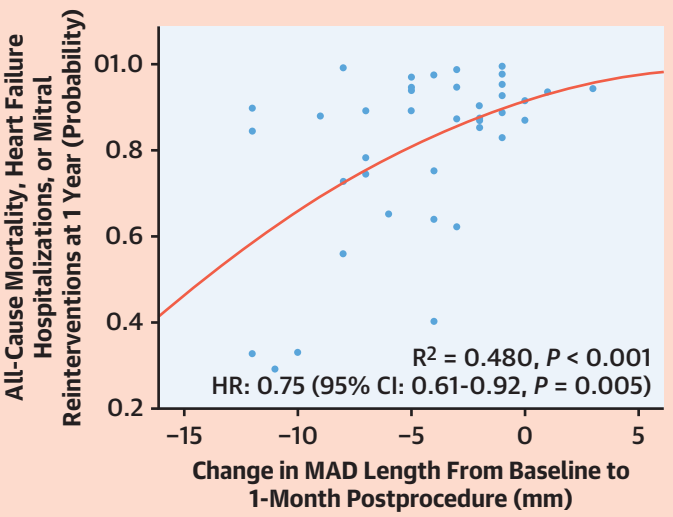
- Longer procedural duration
- More devices per case
- Similarly high technical success rate

Postprocedure

- Comparable echocardiographic results
- Less functional improvement

C Prognostic Implications





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undergoing mitral TEER. Consistent with its previously reported association with multiscallop prolapse, leaflet redundancy, and annular expansion,[2,13,14] MAD was linked in our cohort to bileaflet, greater height-prolapse, longer posterior leaflet, and bigger annulus, ultimately leading to a higher number of deployed clips and a longer procedural time. Importantly, neither baseline MR severity nor TMPG in isolation were indicative of procedural course, as the former was comparable in the 2 study groups and the latter demonstrated no correlation with the number of devices implanted. Notwithstanding the association between MAD—as a likely surrogate of extensive degenerative disease—and TEER difficulty, we observed good overall feasibility, safety, and efficacy irrespective of MAD presence and extent, possibly reflecting operator experience. Further, preferentially multicenter studies are needed to characterize the relationship between MAD and technical aspects of mitral TEER.

Apart from the plausible implications of MAD on MV substrate and procedural characteristics, our study also implies a prognostic function for MAD in the context of mitral TEER. As stressed, patients demonstrating MAD faced a tendency toward a higher cumulative incidence of deaths and a significantly increased risk for mortality and functional incapacitation postprocedure. Furthermore, we showed, for the first time to our knowledge, that a reduction in MAD length following TEER was associated with a more favorable course, as expressed in greater freedom from deaths, HF hospitalizations, or mitral reinterventions—all independent of other echocardiographic parameters at baseline and measures of procedural success at 1 month. The mechanism underlying these observations was unclear. Apparently, MR- and HF-related processes did not play a role, in view of the intergroup similarities in baseline clinical characteristics, postinterventional echocardiographic results, and medical treatment. Likewise, the higher number of clips used in patients with MAD, which previously has been shown to confer worse prognosis in unselected TEER cases,[15] was not associated with outcomes in our cohort. Theoretically, the adverse implications of MAD could have represented the more advanced degenerative valvular disease, thus implying MAD as an "innocent bystander." In this sense, given that leaflet redundancy, as observed in the MAD group, has been previously linked with ventricular ectopy,[2] that excess mortality among patients with MAD in our study primarily resulted from deaths of unknown cause, and that routine continuous rhythm monitoring beyond the hospitalization phase was not performed, it is conceivable that arrhythmic phenomena directly contributed to our observations. Yet, the fact that the predictive ability of MAD, both preprocedurally and postprocedurally, was unaffected by paralleling measures of valve degeneration implies MAD as a potentially independent prognostic marker.

On a final note, our results suggest that mitral TEER, in addition to its proven utility in the treatment of MR, may also address MAD. Like observations made in surgical cohorts,[13,14,16,17] we detected a significant shortening overall and a net reduction in the great majority of patients in MAD length from baseline to 1 month post-TEER. Although readily explained by direct annular manipulation (eg, suturing) in the context of a surgical intervention, the reason for MAD regression following percutaneous repair is less obvious. One explanation may lie in reduced leaflet mobility and redundancy and/or genuine annular "migration," all brought about by leaflet approximation and associated traction forces culminating in an "annuloplasty-like" effect.[18] Consistent with this assumption was the higher number of deployed clips and smaller LV following TEER among those with vs without a ≥50% reduction in MAD length, which, perhaps owing to low power, were only nominal and not statistically significant. Another explanation may relate to improved ventricular geometry and mechanics, and specifically pressure-volume relationship,[19,20] which may have also translated to a better biventricular function and hence prognosis following TEER in patients with a more pronounced MAD regression. Lastly, MAD

CENTRAL ILLUSTRATION Continued

Among 271 consecutive patients undergoing transcatheter edge-to-edge repair (TEER) for degenerative mitral regurgitation, mitral annular disjunction (MAD) was common at baseline and regressed in most patients by 1-month (A). The finding's presence, as compared with its absence, was associated with a more advanced degenerative disease and a longer intervention that utilized more devices per case, without impacting technical success and residual regurgitation post-procedure (B). Ultimately, patients with MAD experienced a numerically higher cumulative incidence and a significantly higher risk of death along the first postprocedural year (C). Conversely, shortening of the aberration at 1 month was prognostically beneficial in regard to the risk of all-cause mortality, heart failure hospitalizations, or mitral reinterventions at 1 year.

shortening post-TEER could, at least partially, be the consequence of measurement errors, originating in baseline overestimation (caused by leaflet redundancy) and postprocedural underestimation (resulting from foreign body–related artifacts). However, neither accompanying markers of degenerative disease nor the number of deployed clips affected the prognostic significance of MAD, and preprocedural MAD extent was not associated with MAD change after TEER, all arguing against misassessment being the sole generator of our findings. Once again, future, larger studies incorporating invasive hemodynamic assessment and noninvasive tissue characterization may elucidate the cause of this impact of TEER on MAD, as well as its predictors.

STUDY LIMITATIONS. First, the single-center, single-arm, retrospective design of the study, along with the small absolute sample size of selected cases perceived to be appropriate for mitral TEER, may hamper generalizability of results. However, our cohort constituted the largest to date in relative terms, resembled the larger Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies Registry of degenerative MR patients treated by TEER,[21] and was analyzed using blinded echocardiographic readings, thus enhancing validity. Second, incomplete data regarding echocardiographic measurements and functional status at 1 month and 1 year, as well as the low number of observed events, may have all interfered with the interpretation of results, facilitating type 1 errors and making some of the total cohort and all of the subgroup analyses exploratory. Nevertheless, data availability was similar in the various groups and subgroups and consistent with recent reports;[12,22] did not affect the Kaplan-Meier and regression analyses; was not associated with MAD status at baseline or its change at 1- month; and did not encompass primary outcome elements, which were monitored in all patients regardless of follow-up location. Third, the assessment of MAD by 2D TTE may be prone to patient-, operator-, and interpreter-related bias, especially in the presence of artifacts characterizing the postprocedural stage. Furthermore, the ability of 2D TTE to differentiate between the newly proposed entities of "true" MAD (which should manifest throughout the cardiac cycle) and "pseudo" MAD (which, representing leaflet redundancy rather than actual annular hinge aberration, is expected to appear in systole only) is inherently limited compared with tomographic and histopathologic studies upon which these entities were hypothesized, thus potentially leading to misappreciation of the burden of the condition.[23] Yet, our approach was in line with previous publications and consensus statement; demonstrated an acceptable level of interobserver agreement and thus reproducibility; allowed for a reliable comparison of the pre- and postprocedural phases; and is simpler and more applicable to everyday clinical practice. Fourth, guideline-directed HF therapy was suboptimal. Although corresponding to patients' tolerance and comorbidities, and reflecting the real-world setting of the study,[24] this may limit the extrapolation of our results to medically optimized patients. Lastly, our findings represent a relatively short-term duration of follow-up and may not apply to non-MitraClip systems nor to MAD patients free of significant MR, the latter of whom are not considered eligible for intervention by current standards.

CONCLUSIONS

In our high-volume, single-center cohort of patients undergoing TEER for degenerative MR, MAD was highly prevalent and marked a more complex valvular anatomy and intervention, as well as a slightly less favorable postprocedural clinical course. Among patients with available 1-month data, a shortening of MAD after TEER was seen in most cases and associated with improved outcomes. These findings suggest MAD as a clinically meaningful factor in this population.

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Dr Chakravarty is a consultant for Edwards Lifesciences, Abbott Lifesciences, Boston Scientific, and Medtronic; is a speaker for Edwards Lifesciences, Boston Scientific, and Medtronic; and is a proctor for Edwards Lifesciences and Medtronic. Dr Makkar has received grant support from Edwards Lifesciences Corporation; is a consultant for Abbott Vascular, Cordis, and Medtronic; and holds equity in Entourage Medical. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? MAD is a common finding in patients with mitral valve prolapse. Its prognostic role is ill-defined among those undergoing TEER.

WHAT IS NEW? In our single-center, 271-case experience, MAD affected 22.9% of patients and was associated with larger valves, a more diffuse prolapse, and increased procedural complexity. While technical success and structural results were not affected by MAD status, mortality and functional incapacity risks following TEER were higher among those with MAD and greater MAD length, respectively. At 1-month post-procedure, MAD regressed in most patients with available data, and the extent of regression correlated with improved outcomes.

WHAT IS NEXT? Further research is needed to characterize the mechanism(s) underlying the complex, presumably bidirectional interaction between MAD and mitral TEER.

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KEY WORDS MitraClip, mitral annular disjunction, mitral regurgitation, mitral transcatheter edge-to-edge repair, transcatheter mitral valve repair

APPENDIX For supplemental figures and tables, please see the online version of this paper.