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ORIGINAL RESEARCH

Impact of Atrial Fibrillation in Patients With Severe Mitral Regurgitation Undergoing Transcatheter Edge-to-Edge Repair

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BACKGROUND: Atrial fibrillation (AF) and mitral regurgitation (MR) are closely linked, and one may worsen the other. We investigated the impact of baseline AF in patients with MR undergoing transcatheter edge-to-edge repair.

METHODS: One-hundred-fifty-six consecutive patients with symptomatic heart failure (HF) undergoing mitral valve transcatheter edge-to-edge repair for severe MR were studied. The primary end point was the composite outcome of death or HF hospitalization. Transthoracic echocardiograms were performed at baseline and follow-up.

RESULTS: Mean age was 80.8±8.8 years and 82 (52.6%) patients were female. MR cause was primary in 69 (44.2%) and secondary in 87 (55.8%) patients. AF or atrial flutter was present in 59 (37.8%) patients at baseline. Mitral valve transcatheter edge-to-edge repair was successful (≤2+ MR) in 58 (98.3%) and 94 (96.9%) patients with and without AF respectively (P=0.59). During median 12.5 months follow-up, the primary end point occurred in 64 patients (2-year Kaplan–Meier estimated rate 41.0%), including death in 16 patients (10.3%) and HF hospitalization in 57 patients (36.5%). Baseline AF remained a significant independent predictor of death or HF hospitalization (adjusted hazard ratio, 2.03 [95% CI, 1.12–3.69], P=0.02). Left ventricular end-diastolic volume, left atrial volume, and right ventricular systolic pressure decreased during follow-up among patients in sinus rhythm but not among those in AF. AF was associated with an increased risk of severe MR recurrence (18.6% versus 8.2%, P=0.05).

CONCLUSIONS: In patients with HF and severe MR treated with Mitral valve transcatheter edge-to-edge repair, baseline AF was associated with impaired right and left heart remodeling, more frequent MR recurrence, and more than doubling of the 2-year risk of death or HF hospitalization.

Key Words: atrial fibrillation ■ death ■ heart failure ■ heart remodeling ■ mitral regurgitation ■ transcatheter mitral valve edge-to-edge repair

Mitral regurgitation (MR) is the second most common valvular disease, affecting an estimated 2% to 3% of the general population and up to 10% of those >75 years of age.[1] Severe MR is associated with increased morbidity and mortality, underscoring the need for effective intervention. Mitral valve transcatheter edge-to-edge repair (M-TEER) has emerged as a minimally invasive, safe, and effective approach to treating

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CLINICAL PERSPECTIVE

What Is New?

- Atrial fibrillation (AF) and mitral regurgitation are closely linked, and one may worsen the other; however, the impact of AF in patients with heart failure and severe mitral regurgitation undergoing transcatheter edge-to-edge repair is unclear.

What Are the Clinical Implications?

- Despite comparable acute results as in patients with sinus rhythm, baseline AF at the time of the procedure was associated with more than doubling of the risk of death or heart failure hospitalization during 2-year follow-up.
- AF was associated with impaired cardiac remodeling, particularly in the left ventricle, left atrium, and right ventricle, within the first year after the procedure.
- Patients with AF also had more frequent recurrence of severe mitral regurgitation during follow-up.

Nonstandard Abbreviations and Acronyms

HFH	heart failure hospitalization
MR	mitral regurgitation
M-TEER	mitral valve transcatheter edge-to-edge repair
SR	sinus rhythm

severe MR, especially in patients with secondary (functional) MR due to heart failure (HF). In an older patient population with HF and severe secondary MR who remained symptomatic despite maximally tolerated guideline directed medical therapy enrolled in the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial, M-TEER markedly reduced the rates of HF hospitalizations (HFH) and all-cause mortality during 5-year follow-up.[2,3] M-TEER is also useful in patients with primary (degenerative) MR who are at high-risk for surgical repair.[4] Although surgical treatment for primary MR is still considered the gold standard treatment for lower risk patients with primary MR,[5] 2 prospective randomized trials (clinicaltrials.gov NCT04198870 and NCT05051033) are currently ongoing to investigate the effect of M-TEER in lower risk patients with primary MR.

The prevalence of atrial fibrillation (AF), the most common cardiac arrhythmia, is increased in an aging population and often coexists with MR.[6] The 2 conditions are closely linked—MR may contribute to AF development through left atrial (LA) volume overload while AF may cause or worsen MR through mitral annular dilation or leaflet tethering.[7] Although concomitant AF has been shown to worsen the prognosis of patients undergoing surgical mitral valve repair,[8] the impact of AF on outcomes after M-TEER is not well defined, with studies to date yielding conflicting results.[9,10] To further explore this issue, we investigated the impact of AF on clinical outcomes in patients with severe secondary MR undergoing M-TEER.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design

Consecutive patients aged 18 years or older referred for M-TEER at a single academic medical center (Mount Sinai Fuster Heart Hospital, New York, NY) between January 2021 and December 2023 with severe (grade 3+ or 4+) MR were included.

All participants underwent comprehensive 2-dimensional and Doppler transthoracic echocardiography at baseline and during follow-up using commercially available ultrasound systems. For patients with multiple echocardiograms during follow-up, the values from the last available study before the end of follow-up were used. Conventional echocardiographic parameters were measured in accordance with the guidelines established by the American Society of Echocardiography.[11,12] The severity of MR and decision to perform M-TEER were determined by consensus of a multidisciplinary heart team. Echocardiograms were interpreted by a structural echocardiographer (S.L.) with measurements performed without knowledge of the patients' clinical features.

The history, baseline clinical characteristics, and echocardiographic and procedural details were recorded by treating physicians and extracted from electronic medical records. AF was defined by its presence on the ECG performed on the day of the M-TEER procedure before intervention. The observation period began on the date of intervention and continued until the last follow-up visit or death.

The study was approved by the institutional review board at the Icahn School of Medicine at Mount Sinai. Informed consent was waived due to the retrospective nature of the investigation.

End Points

The primary end point of interest was the composite of all-cause mortality or HFH after M-TEER. Secondary

end points were the individual components of the composite end point and changes in echocardiographic parameters, including left ventricular (LV) end-diastolic volume index, LV end-systolic volume index, LV ejection fraction, LV mass index, left atrial volume index (LAVI), right ventricular systolic pressure (RVSP), and MR recurrence at follow-up.

Follow-up data were obtained through review of medical records. Deaths were confirmed through cross-referencing with the Limited Access Death Master File. Data from patients lost to follow-up were censored at the time of last known contact. Periprocedural complications were defined in accordance with the Valve Academic Research Consortium-3 definitions.[13]

Statistical Analysis

Continuous variables were expressed as the median and interquartile range and categorical variables as values and percentages. Baseline and echocardiographic characteristics were assessed using the Kruskal–Wallis test, Mann–Whitney *U* test, and Pearson's chi-square statistics. The Wilcoxon signed-rank test for paired samples was used to analyze changes in echocardiographic parameters, and McNemar's test was used to analyze the change in New York Heart Association functional classification after M-TEER, compared with baseline. Kaplan–Meier methodology was used to construct time-to-first event curves, and the differences between groups were assessed using the log-rank test. Multivariable analysis was performed to investigate the independent association of AF with the primary composite outcome after M-TEER. Covariates included in the multivariable models were selected based on prior studies that established variables associated with mortality and HF outcomes.[14,15] To evaluate changes in echocardiographic parameters by AF status while accounting for variability in follow-up echocardiography timing, we performed linear regression analyses modeling the change in each echo variable as the outcome. Each model included AF status, the baseline value of the corresponding variable, and time to follow-up echocardiography as covariates. We also tested for an interaction between AF status and follow-up time. Estimates are reported as hazard ratio (HR) and 95% CIs. A 2-tailed *P* value <0.05 was considered statistically significant for all analyses. All statistical analyses were performed with STATA v19, (Stata Corp, College, TX).

RESULTS

Between January 2021 and August 2023, 156 consecutive patients with severe MR underwent M-TEER. AF was present in 59 patients (37.8%) and sinus rhythm (SR) was present in 97 (62.2%) patients (including 37 patients with a prior history of AF who were in SR at the time of the M-TEER procedure). Baseline clinical characteristics and medication use stratified by the presence of AF are shown in Table 1. Mean age was 80.8±8.8 years, 82 (56.6%) were female, and all patients were symptomatic, with 140 (89.7%) in New York Heart Association class III. Most baseline characteristics were similar in patients with and without AF, except that those with AF were more likely to have secondary MR (43 [72.9%] versus 48 [49.5%], *P*=0.004), higher body mass index, and history of stroke. At the time of the procedure, patients with AF were clinically stable and were more frequently treated with beta blockers (86.4% versus 68.0%, *P*=0.03) and loop diuretics (79.7% versus 63.9%, *P*=0.04) compared with those in SR. Patients with AF had similar LV volumes and LV ejection fractions, but a larger LAVI and more frequent tricuspid regurgitation of at least moderate severity, despite similar RVSP compared with patients in SR (Table 2). Conversely, the quantitative severity of MR as measured by the effective regurgitant orifice area and regurgitant volume were greater in patients in SR (*P*=0.06 and *P*=0.04, respectively).

Procedural Outcomes Stratified by the Baseline Rhythm

Table 3 summarizes the transesophageal echocardiographic findings after M-TEER. M-TEER was equally successful in patients with AF and SR in achieving moderate or less (0 to 2+) MR (58 [98.3%] versus 94 [96.9%], respectively, *P*=0.59) and mild or less (0 or 1+) MR (55 [93.2%] versus 84 [86.6%], respectively, *P*=0.20).

Clinical Outcomes After M-TEER Stratified by the Baseline Rhythm

Median follow-up was 12.5 (5.4–17.4) months (13.2 [4.2–21.8] for AF versus 11.5 [6.0–17.4] months for SR, *P*=0.38). One-year follow-up was performed in 60/97 (61.9%) patients in SR and in 29/59 (49.2%) patients with AF; the remaining patients had shorter follow-up durations. The primary end point occurred in 64 patients (2-year Kaplan–Meier estimated rate 41.0%), including death in 16 patients (10.3%) and HFH in 57 patients (36.5%). At 2 years, death or HFH had occurred in 31 (52.5%) of patients with AF versus 32 (33.0%) with SR (unadjusted HR, 1.88 [95% CI, 1.14–3.08], *P*=0.01) (Figure 1A). Mortality occurred more frequently in patients with AF compared with SR (9 [15.3%] versus 7 [7.1%]; unadjusted HR, 2.30 [95% CI, 0.86–6.18], *P*=0.10), as did HFH (28 [47.5%] versus 29 [29.9%]; unadjusted HR, 1.71 [95% CI, 1.02–2.88], *P*=0.04) (Figure 1B and 1C). The differences between the groups in the rates of stroke were not significant

Table 1. Baseline Clinical Variables and Medication Use Stratified by the Presenting Rhythm

	SR present (n=97)	AF present (n=59)	*P* value
Age, y	80.3 (74.0–87.5)	81.8 (78.0–86.0)	0.30
Male sex	42 (43.3)	32 (54.2)	0.19
Race and ethnicity			0.23
White	52 (53.6)	37 (62.7)	
Black	10 (10.3)	4 (6.8)	
Hispanic	6 (6.2)	7 (11.9)	
Other	29 (29.9)	11 (18.6)	
Cause of mitral regurgitation			0.004
Primary	49 (50.5)	16 (27.1)	
Secondary	48 (49.5)	43 (72.9)	
History of AF	37 (38.1)	59 (100.0)	<0.001
Body mass index, kg/m^2	24.7 (21.2–27.1)	26.8 (22.4–28.5)	0.04
History of smoking	22 (22.7)	13 (22.0)	0.90
Coronary artery disease	61 (62.9)	35 (59.3)	0.66
History of coronary artery bypass graft	24 (24.7)	12 (20.3)	0.53
History of percutaneous coronary intervention	39 (40.2)	16 (27.1)	0.09
History of cerebrovascular accident	13 (13.4)	16 (27.1)	0.03
Peripheral artery disease	18 (18.6)	14 (23.7)	0.44
Hypertension	88 (90.7)	57 (96.6)	0.16
Hyperlipidemia	80 (82.5)	50 (84.7)	0.71
Diabetes	30 (33.0)	23 (39.0)	0.30
Chronic obstructive pulmonary disease	23 (23.7)	10 (16.9)	0.32
EuroScore II, %	5.1 (2.9–6.0)	6.6 (3.1–7.6)	0.08
6-minute walk distance, m	511.1 (400.0–650.0)	537.3 (412.5–650.0)	0.43
Brain natriuretic peptide, pg/mL	362.3 (146.4–799.3)	502.2 (321.8–852.3)	0.08
N-terminal pro-B-type natriuretic peptide, pg/mL	3865.5 (1888.3–8838.3)	2059.0 (1087.5–5605.8)	0.24
Serum creatinine, mg/dL	1.5 (0.9–1.5)	1.4 (0.9–1.7)	0.58
Creatinine clearance, calculated by the Modification of Diet in Renal Disease formula ≤60 mL/min per 1.73 m^2	57 (58.8)	39 (66.1)	0.40
New York Heart Association class			0.25
II	12 (12.4)	5 (8.5)	
III	76 (78.4)	52 (88.1)	
IV	9 (9.3)	2 (3.4)	
Antiplatelet agents	57 (58.8)	19 (32.2)	<0.001
Anticoagulation	35 (36.1)	48 (81.4)	<0.001
Beta blockers	66 (68.0)	51 (86.4)	0.03
Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers	37 (38.1)	30 (50.8)	0.12
Angiotensin receptor/ neprilysin inhibitor	19 (19.6)	14 (23.7)	0.54
Sodium-glucose cotransporter-2 inhibitors	18 (18.6)	13 (22.0)	0.60
Loop diuretics	62 (63.9)	47 (79.7)	0.04
Mineralocorticoid receptor antagonist	27 (27.8)	19 (32.2)	0.56
Statin	71 (73.2)	48 (81.4)	0.29

Values are presented as median (25th–75th percentile) or n (%). AF indicates atrial fibrillation/flutter; and SR, sinus rhythm.

(Figures 1D). By multivariable analysis, AF remained a significant independent predictor of death or HFH during follow-up (HR, 2.03 [95% CI, 1.12–3.69], *P*=0.02) (Table 4).

Echocardiographic Changes During Follow-Up

Follow-up echocardiography was completed in 147/156 patients (94.2%) at a median time of 6.0 (1.0–12.2) months (12.0 [1–14.3] for AF versus 7 [1–12 months] for SR, *P*=0.18). As shown in Figure 2, LV end-diastolic volume index, LAVI, and RVSP decreased during follow-up only in patients with SR, whereas RVSP increased in those with AF. LV end-systolic volume index and LV mass index decreased in both groups, whereas LV ejection fraction remained unchanged. Patients with AF compared with SR were more likely to have severe (3+ or 4+) MR at follow-up (18.6% versus 8.2%, *P*=0.05) (Figure 3). No significant interactions between AF status and follow-up duration were observed for changes in echocardiographic parameters.

Sensitivity Analyses

Of note, although no deaths occurred during the index hospitalization, 12 events (4 deaths and 8 HFHs) occurred within 30 days of the procedure (5 events in patients in SR and 7 events in patients in AF). To examine the effect of cardiac rhythm on late outcomes, we performed a landmark analysis beginning at 30 days. AF remained associated with adverse outcomes between 30 days and 2 years (adjusted HR [aHR], 2.95 [95% CI, 1.27–6.87], *P*=0.01) (Figure S1, Table S1).

A sensitivity analysis was also performed including all patients with a documented history of AF in the group with AF, regardless of rhythm at the time of the procedure. In this analysis 96 patients with a history of AF (including 59 with AF at the time of the procedure and 37 patients with a history of AF who were in SR at the time of the procedure) were compared with 60 patients in SR who had no history of prior AF.

Table 2. Baseline Echocardiographic Parameters Stratified by the Presenting Rhythm

	SR present (n=97)	AF present (n=59)	*P* value
LV end-diastolic volume index, mL/m^2	79.9 (52.0–99.0)	71.5 (50.5–78.3)	0.15
LV end-systolic volume index, mL/m^2	43.1 (20.0–58.3)	37.0 (20.3–43.0)	0.25
LV ejection fraction, %	51.2 (40.0–64.5)	49.9 (40.0–60.3)	0.58
≤40%	26 (26.8)	43 (72.9)	<0.001
>40%	71 (73.2)	16 (27.1)	<0.001
Interventricular septum thickness, cm	1.1 (0.9–1.2)	1.1 (1.0–1.3)	0.09
LV posterior wall thickness, cm	1.0 (0.9–1.1)	1.1 (0.9–1.2)	0.03
Left atrial volume index, mL/m^2	57.2 (43.0–66.7)	87.9 (58.9–101.9)	<0.001
E wave, cm/s	105.6 (84.5–130.3)	134.5 (89.0–115.0)	0.24
E′ wave, cm/s	11.6 (4.0–6.6)	6.8 (5.5–8.2)	0.61
E/E′	18.7 (13.0–23.2)	14.1 (8.6–17.9)	0.007
LV mass index, g/cm^2	115.8 (88.0–142.0)	118.0 (94.9–141.0)	0.71
≥Moderate tricuspid regurgitation	42 (42.3)	46 (78.0)	<0.001
Right ventricular systolic pressure, mm Hg	46.1 (34.0–55.5)	48.0 (36.8–58.8)	0.49
Pulmonary vein flow			0.28
0/1+	4/90 (4.4)	0/54 (0.0)	
2+	54/90 (60.0)	35/54 (64.8)	
3+/4+	32/90 (53.6)	19/54 (35.2)	
Effective regurgitant orifice area, cm^2	0.53 (0.35–0.61)	0.48 (0.31–0.56)	0.06
Regurgitant volume, mL	83.8 (58.3–101.8)	70.7 (52.0–81.5)	0.04
MR grade 3+	5 (5.2)	5 (8.5)	0.41
MR grade 4+	88 (90.7)	51 (86.4)	0.40
Mitral valve area, cm^2	5.1 (4.3–5.8)	5.6 (4.5–6.8)	0.06

Values are presented as median (25th–75th percentile) or n (%). AF indicates atrial fibrillation; LV, left ventricular; MR, mitral regurgitation; and SR, sinus rhythm.

Tables S2 and S3 show the baseline clinical and echocardiographic parameters based on history of AF. In this analysis, a history of AF was associated with an increased risk of death or HFH in univariable analysis (HR, 1.82 [95% CI, 1.05–3.14], *P*=0.03) (Figure S2). However, this association was no longer significant after adjustment for clinical covariates (aHR, 1.78 [95% CI, 0.93–3.42], *P*=0.08) (Table S4).

DISCUSSION

In this study, patients with AF at the time of M-TEER had worse cardiovascular outcomes than those in SR at baseline, with increased risk of both death and HFH during 2-year follow-up. There were no differences in the incidence of stroke. Patients with SR also had favorable LV, LA, and RV remodeling during follow-up, as indicated by improved LV end-diastolic volume index, LAVI, and RVSP, whereas patients in AF did not. Finally, patients with AF had more severe MR and worse RVSP after during follow-up. By multivariable analysis, AF remained a significant independent predictor of death or HFH during follow-up after M-TEER.

Current clinical practice guidelines recommend mitral valve repair when possible for asymptomatic patients with severe primary (degenerative) MR who develop AF with preserved LV size and function and AF.[16] M-TEER is reserved for patients at high or prohibitive risk for surgery but is increasingly used in lower risk patients as well.[17] The results of the COAPT, MITRA-FR (MitraClip Device for Severe Functional/Secondary Mitral Regurgitation), and RESHAPE-HF2 (Transcatheter Valve Repair in Heart Failure With Moderate to Severe Mitral Regurgitation) trials support M-TEER as the primary approach for patients with severe secondary (functional) MR. However, whereas the adverse impact of preoperative AF on patients undergoing surgical MV repair has been established,[18] the impact of this arrhythmia after M-TEER is less clear. A multicenter study across 5 centers in the Netherlands analyzing 618 patients who underwent M-TEER reported that mortality and MR recurrence were similar among those with and without baseline AF at 1-year follow-up.[9] Similarly, in EVEREST II (Endovascular Valve Edge-to-Edge Repair Study), there was no difference in all-cause mortality between patients with and without AF.[19] Conversely, data from the TVT (Transcatheter Valve Therapy) and TRAMI (Transcatheter Mitral Valve Interventions) registry showed worse survival at 12 months for patients with AF after M-TEER.[15,20]

Table 3. M-TEER Procedural Outcomes Stratified by the Presenting Rhythm

	SR present (n=97)	AF present (n=59)	*P* value
Number of clips >1, %	36 (37.1)	22 (37.3)	0.59
Mean gradient, mm Hg	3.0 (2.0–4.0)	3.0 (2.0–4.0)	0.21
>5 mm Hg	10 (10.3)	3 (5.1)	0.25
Mitral regurgitation grade			
0/1+	84 (86.6)	55 (93.2)	0.20
2+	10 (10.3)	3 (5.1)	0.25
3+/4+	3 (3.1)	1 (1.7)	0.59
Pulmonary vein flow			0.37
0/1+	58/87 (66.7)	33/48 (68.8)	
2+	29/87 (33.3)	14/48 (29.2)	
3+/4+	0/87 (0.0)	1/48 (2.1)	

Values are presented as median (25th–75th percentile) or n (%). AF indicates atrial fibrillation; M-TEER, mitral transcatheter edge-to-edge repair; and SR, sinus rhythm.

In contrast to most prior reports, in our study, AF was defined based on the rhythm documented on the ECG performed on the day of and before the M-TEER procedure, maximizing the risk that AF might be deleterious (as opposed to a remote history of AF that might not recur). Nonetheless, a successful M-TEER procedure was achieved equally in patients with SR and AF. However, our study confirmed an independent risk of AF on the composite outcome of all-cause death or HFH due to increased risk of both mortality and HFH during 2-year follow-up compared with the outcomes observed in patients in SR at the time of M-TEER. The negative effect of baseline AF was especially evident beyond 30 days after the M-TEER procedure and was reflected in greater risk of death and HFH as well as worse LV remodeling, increase in RVSP and greater recurrent severe MR. Compared with the EVEREST II trial, our cohort represented a higher-risk population, with older age (mean 80.8 versus 68.5 years), lower LV ejection fraction (50.6% versus 60%), and a greater proportion of patients in New York Heart Association functional class III/IV (89.1% versus 49.2%).[19] These differences likely contributed to the higher observed mortality in our study, consistent with the expectations of real-world clinical data as opposed to a controlled trial population. Also of note, patients with AF at baseline likely had a higher burden of AF than the broader group of patients with a history of AF that included patients with prior paroxysmal AF who were in SR at the time of the M-TEER procedure. This likely explains why AF at baseline was an independent predictor of death or HFH after M-TEER, whereas any history of AF was not.

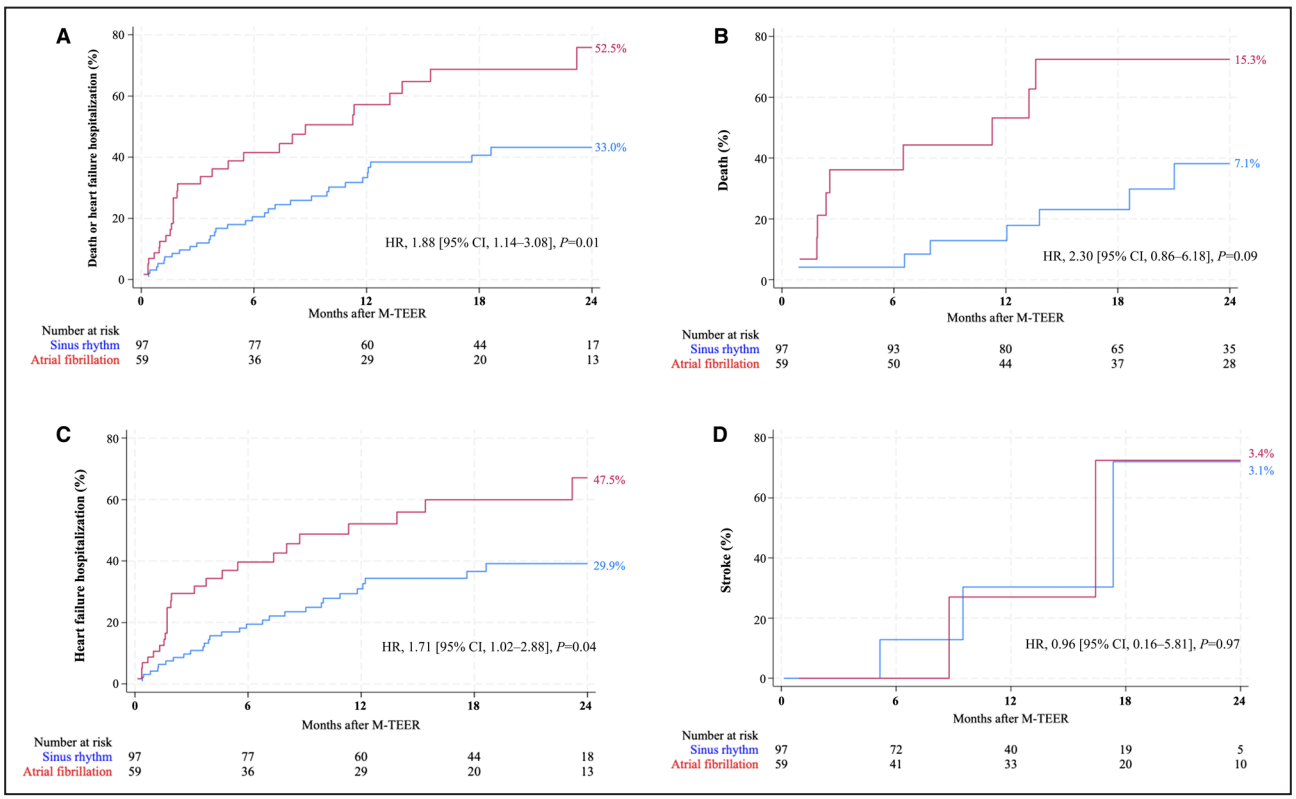

Figure 1. Time-to-first event rates during follow-up stratified by baseline rhythm.
A, Death or HFH. **B**, Death. **C**, HFH. **D**, Stroke. HFH indicates heart failure hospitalization; HR, hazard ratio; and M-TEER: mitral transcatheter edge-to-edge repair.

Table 4. Baseline Predictors of the Primary Composite Outcome of Death or HFH After M-TEER

	Adjusted HR (95% CI)	*P* value
Age, per 1-y increase	0.98 (0.94–1.01)	0.20
Sex, female	1.03 (0.57–1.88)	0.92
History of smoking	0.81 (0.36–1.80)	0.60
Hypertension	0.99 (0.32–3.10)	0.99
Diabetes	1.00 (0.52–1.94)	0.99
Chronic obstructive pulmonary disease	1.42 (0.75–2.68)	0.28
Peripheral arterial disease	1.84 (0.85–3.99)	0.12
New York Heart Association class ≥3	1.48 (0.51–4.26)	0.47
Effective regurgitant orifice area index, per 0.1 cm^2/m^2 increase	1.24 (0.47–3.28)	0.66
LV end-diastolic volume index, per 10 mL/m^2 increase	0.99 (0.99–1.01)	0.64
Atrial fibrillation at baseline	2.03 (1.12–3.69)	0.02
EuroScore (per 1% increase)	1.03 (0.98–1.08)	0.19
Chronic kidney disease	2.07 (1.08–3.98)	0.03
LV ejection fraction ≤40%	1.16 (0.52–2.60)	0.71

HFH indicates heart failure hospitalization; HR, hazard ratio; LV, left ventricular; and M-TEER: mitral transcatheter edge-to-edge repair.

The mechanisms responsible for the worse cardiovascular outcomes in patients with AF undergoing M-TEER are uncertain but may be related to structural and functional echocardiographic differences after the intervention. Prior evidence suggested that the adverse consequences in patients with a history of AF may be related to differences in demographic and clinical characteristics at baseline, such as older age,[9,15] chronic kidney disease,[21] or more advanced valvular disease.[22] In our study we did not see differences in patient age or valvular disease severity in those with AF and SR. Rather, patients with SR exhibited more favorable LV, LA, and RV remodeling after M-TEER indicated by lower LV end-diastolic volume index, LAVI, RVSP, and MR ≥2 recurrence within 6 to 12 months after the M-TEER procedure. Mean RSVP also decreased during follow-up after M-TEER in patients with SR but increased in those with AF, likely contributing to their worse prognosis. Our results confirm prior findings that suggested more favorable LA and LV remodeling in patients in SR[19]; however, we also found a higher risk of severe MR recurrence at follow-up compared with prior studies,[9] possibly due to a higher prevalence of a primary MR in our cohort.

The development of AF in the patient with MR may reflect worse structural and functional MR severity and unfavorable LA, LV, and RV remodeling in response to the valve lesion.[7] Our study suggests AF may also indicate a relatively worse prognosis after M-TEER compared with that expected in patients with SR. Similarly, patients with recurrent AF after catheter ablation had greater LA dilation and MR than those in whom SR was sustained.[23] Rhythm control has been proposed as a means of promoting atrial reverse remodeling and restoring atrioventricular coupling.[24–26] Prior evidence has advocated surgical MV repair to avoid the detrimental effects of AF.[27] To date, no data are available regarding whether M-TEER reduces the future incidence or burden of AF. The present study warrants the need for adjuvant strategies to optimize outcomes in patients with established AF undergoing transcatheter MV repair. In this regard surgical ablation for AF has become common during MV surgery and has been shown to improve prognosis.[28]

The TVT registry reported an increased risk of stroke within the first year after M-TEER in patients with AF compared with SR.[29] In contrast, we found no difference in the incidence of stroke between patients with SR and AF, possibly due to a higher prevalence of anticoagulant therapy in our cohort than in the TVT registry (81.4% versus 62.6%).

Strengths and Limitations

To our knowledge the present study is the first to comprehensively evaluate the impact of AF at the time of the procedure on the risk of HF, mortality, and subsequent cardiac function and structural remodeling following M-TEER in patients with severe primary and secondary MR. Careful use of multivariable modeling was used to adjust for covariates that might be common with AF and otherwise impair prognosis. However, several limitations should be noted. First, the study population predominantly included older adults, which is representative of patients who most commonly undergo M-TEER; therefore, our results may not apply to younger individuals. Second, the retrospective and observational design of the study may not have identified all confounders and limits the ability to establish a cause–effect relationship. Third, the single center nature of our study and modest sample size and number of events limits its generalizability and robustness, with replication needed from additional centers and in more patients. Similarly, we were not adequately powered to determine whether an incremental risk was present in patients with SR at the time of M-TEER who had a prior history of AF. Fourth, the SR group included patients with a history of AF; in this group the duration of SR and the burden of prior AF were unknown, and of course some patients in SR without a prior history of AF may indeed have had AF at some point. The impact of these uncertainties is unknown. Fifth, although the effect size of AF was similar in the primary analysis and a sensitivity analysis in which

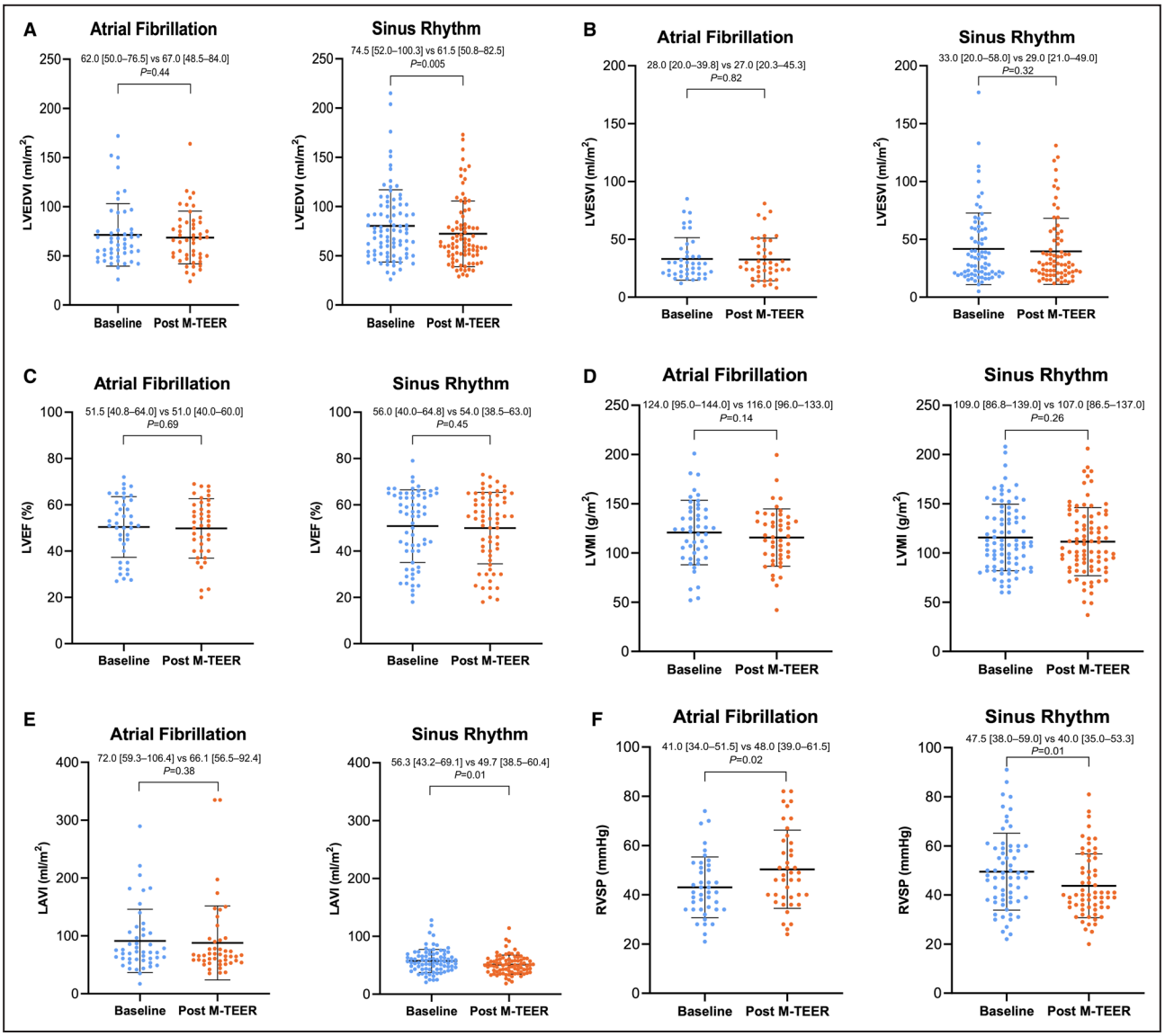

Figure 2. Transthoracic echocardiographic parameters at baseline and follow-up stratified by baseline rhythm.
A, LVEDVI. **B**, LVESVI. **C**, LVEF. **D**, LVMI. **E**, LAVI. **F**, RVSP. LAVI indicates left atrial volume index; LVEDI, left ventricular end-diastolic volume index; LVEF, lLeft ventricular ejection fraction; LVESI, left ventricular end-systolic volume index; LVMI, left ventricular mass index; M-TEER: mitral transcatheter edge-to-edge repair; and RVSP, right ventricular systolic pressure.

patients in SR with a history of AF were included in the group with AF, in the latter analysis the risk of AF did not reach significance, possible representing a type II error. Further studies are required to determine if patients with SR and a history of AF are at intermediate risk between those with AF at the time of the procedure and those without any history of AF. Sixth, although we adjusted for baseline values, we cannot exclude that regression to the mean did not affect the change in echo parameters over time. Finally, AF was not captured during follow-up, and thus the present analysis does not account for the impact of recurrent AF in patients with SR (or conversion to SR in patients with AF).

CONCLUSIONS

In patients with HF and severe MR undergoing M-TEER, despite comparable acute results as in patients with SR, baseline AF at the time of the procedure was associated with more than doubling of the risk of death or HFH during 2-year follow-up. These results were less pronounced in patients with a history of AF.

Patients with AF at the time of the M-TEER procedure exhibited impaired LV, LA, and RV remodeling during 1-year follow-up and had higher RVSP compared with patients in SR. Patients with AF also had more frequent recurrence of severe MR during follow-up.

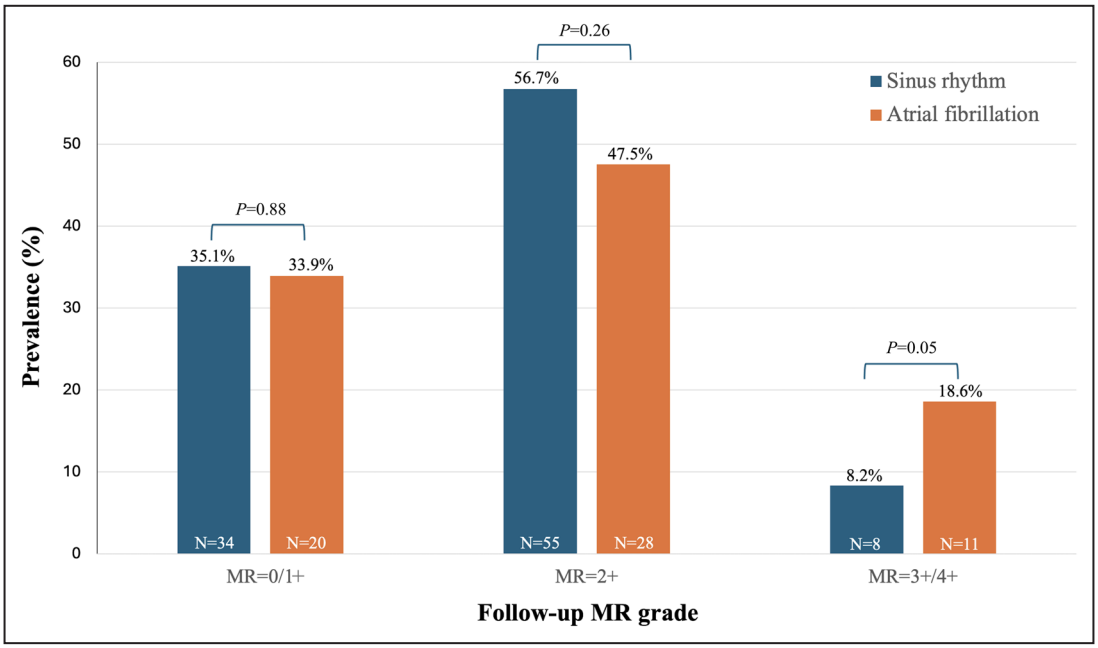

Figure 3. Mitral regurgitation grades from follow-up transthoracic echocardiography stratified by baseline rhythm.
MR indicates mitral regurgitation.

Whether adjunctive rhythm control strategies to prevent or correct AF before or after M-TEER would improve both cardiac function and clinical outcomes requires further investigation.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S4
Figures S1–S2

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