ORIGINAL RESEARCH

Mitral Valve Surgery for Persistent or Recurrent Mitral Regurgitation After Transcatheter Edge-to-Edge Repair Is Associated With Improved Survival

Ahmed El Shaer, MBBS*; Alejandra Chavez Ponce , MD*; Piotr Mazur , MD*; Kevin Greason , MD; Arman Arghami, MD; MD; Mackram F. Eleid , MD; Mayra Guerrero , MD; Charanjit S. Rihal , MD; Juan A. Crestanello , MD[†]; Mohamad Alkhouli , MD[†]

BACKGROUND: The management of severe mitral regurgitation (MR) after transcatheter edge-to-edge repair (TEER) remains a clinical conundrum. Considering the growing volume of TEER, more outcomes data for mitral surgery in this cohort are needed.

METHODS AND RESULTS: Symptomatic patients with persistent or recurrent severe MR after TEER evaluated between May 2014 and June 2021 were included. The primary outcome was all-cause mortality in patients who were treated with surgery versus medical therapy. The Kaplan–Meier and Cox regression methods were used to report risk-adjusted survival analyses. Among the 142 included patients, 44 (31.0%) underwent mitral surgery. Patients who underwent surgery were younger than those treated medically (74.1±8.9 versus 78.6±10.5 years, P=0.01). Major comorbidities were similar except obesity, sleep apnea, left ventricular dimensions, and ejection fraction. Society of Thoracic Surgeons Predicted Risk of Operative Mortality was 9.0±4.7 versus 7.9±4.9 in the surgical versus medical therapy groups, respectively, P=0.22. Time from TEER to detection of severe MR was similar in both groups (median [interquartile range] 97.5 [39.5–384] versus 93.5 [40–389] days in the surgical versus medical groups, respectively [P>0.05]). In the surgical group, valve replacement was performed in all patients. Operative mortality was 4.5% (observed/expected ratio 0.55), and major complications were uncommon. After risk-adjustment, surgery was associated with significantly lower all-cause mortality (adjusted hazard ratio, 0.33 [95% CI, 0.12–0.92], P=0.001) compared with medial therapy.

CONCLUSIONS: Compared with medical therapy, mitral surgery in patients with severe persistent or recurrent MR after TEER is associated with lower mortality despite the high-risk profile of these patients. Patients with severe MR after TEER should be considered for surgery at a referral mitral surgical center.

Key Words: edge-to-edge repair
mitral regurgitation
mitral valve surgery

See Editorial by Zahr and Sweis.

ranscatheter edge-to-edge repair (TEER) is an increasingly used treatment for patients with severe mitral regurgitation (MR) who are at high risk for surgery.^{1–3} Despite its high short-term technical

success, persistent and recurrent severe MR occurs in \approx 5% and 6% to 15% of patients after TEER, respectively.^{2,4-6} With the rising number of TEER procedures, its expanding indications, and its increasing use of

Correspondence to: Mohamad Alkhouli, MD, and Juan A. Crestanello, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905. Email: alkhouli. mohamad@mayo.edu; crestanello.juan@mayo.edu

© 2022 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

JAHA is available at: www.ahajournals.org/journal/jaha

^{*}A. El Shaer, A. Chavez Ponce, and P. Mazur contributed equally.

[†]J. A. Crestanello and M. Alkhouli contributed equally.

For Sources of Funding and Disclosures, see page 10.

CLINICAL PERSPECTIVE

What Is New?

- This study highlights the potential of surgery as an option for high-risk patients who underwent transcatheter edge-to-edge repair and developed recurrent mitral regurgitation.
- The observed-to-expected mortality undergoing mitral valve replacement after failed transcatheter edge-to-edge repair, in a highvolume center, is better than the one reported nationwide.

What Are the Clinical Implications?

- Patients who were initially at high surgical risk for mitral valve replacement could be referred to a high-volume center for surgery after mitral regurgitation recurrence.
- Mitral valve replacement after failed transcatheter edge-to-edge repair represents a feasible option with reduced risk of death.

Nonstandard Abbreviations and Acronyms

MRmitral regurgitationTEERTranscatheter edge-to-edge mitral valve
repair

TEER in complex anatomies (eg, commissural jets, calcified annuli, atrial functional MR, or small valves), concerns have been raised about the management of the growing number of patients with severe MR after TEER.^{7,8} Several studies have shown that persistent or recurrent MR following TEER confers substantially higher morbidity and mortality.^{4,6,9-11} Although mitral valve surgery remains a viable option after failed TEER, many patients may not be referred to surgery because of their high-risk clinical profile. Indeed, a recent nationwide analysis reported a 30-day mortality of 10.2% for mitral surgery after TEER with an observed-to-expected mortality ratio of 1.2, corroborating the concerns about the feasibility of surgical intervention in this high-risk cohort.¹² This study also suggested worse outcomes at low-volume mitral surgery centers, raising the question of whether surgery for failed TEER at a high-volume center would result in more favorable outcomes. Furthermore, to our knowledge, no study to date has compared the outcomes of surgery and optimal medical therapy in this patient cohort. To address these questions, we conducted a comparative analysis of surgical intervention versus medical therapy in patients with severe MR after TEER at a tertiary referral center.

METHODS

Data Availability

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the corresponding author.

Study Cohort

We retrospectively identified patients presenting to the Mayo Clinic, Rochester, Minnesota, with recurrent or persistent MR after mitral TEER with the MitraClip system (Abbott, Abbott Park, IL) between May 2014 and June 2021. We excluded patients who underwent redo MV-TEER (n=17) and patients in our study were deemed ineligible for redo TEER. A total of 72 had functional stenosis. 6 with moderate functional stenosis (mitral gradient \geq 5 mm Hg), and 66 with severe functional stenosis (mitral gradient ≥10 mm Hg). Another 39 patients were excluded owing to the presence of leaflet calcification or insufficient leaflet tissue for leaflet insertion and grasping. The remaining 31 patients were candidates for TEER but did not wish to undergo invasive therapy. Therefore, the study cohort was divided into 2 groups; patients who underwent mitral surgery and those who were treated conservatively (medical treatment arm). The surgical cohort included patients who had their TEER procedure at Mayo Clinic and those who had the procedure done at other centers and were subsequently referred for consideration of surgery.

End Points and Outcomes Measures

The primary end point of this study was risk-adjusted all-cause mortality at maximum follow-up. Secondary end point was the observed-to-expected mortality among patients undergoing surgery. We also described differences in baseline characteristics, MR etiology, predicted risk of mortality, and the time interval between TEER and recurrent MR in both cohorts. Echocardiographic evaluation at the time of recurrent MR was performed at Mayo Clinic, Rochester and MR grading was performed according to the American Society of Echocardiography guidelines. Surgical risk was calculated using the Society of Thoracic Surgeons Predicted Risk of Operative Mortality score (version 2.9) for isolated mitral valve replacement at the time of MR recurrence detection. Patients were usually evaluated with a heart team-based approach that consists of an interventional cardiologist and a cardiac surgeon with expertise in mitral surgery before TEER. Persontime was calculated from the date of first detection of recurrent or persistent MR after TEER to either the latest available follow-up or death. The study was approved by the Mayo Clinic Institutional Review Board. Patient consent requirement was waived as the study was considered a minimal risk retrospective study.

Statistical Analysis

Categorical variables were compared using a chisquare test or Fisher's exact test and presented as frequencies with percentages. Continuous parameters of the study groups were compared using the Student t test. The probability of death according to the treatment strategy (surgery versus medical therapy) was graphically displayed according to the method of Kaplan and Meier, with comparison of cumulative survival across strata by the log-rank test. To adjust for the differences in baseline characteristics a Cox proportional hazards model was created. First a univariate model was built including baseline characteristics that were statistically significantly different between the 2 groups (age, body mass index, sleep apnea, left ventricular [LV] dimensions, LV ejection fraction). All variables with P<0.1 in the baseline characteristics were included in the multivariate model. Hazard ratios (HR) were reported with 95% Cl. Statistical significance was inferred at P≤0.05. All statistical analysis was performed using R Statistical Software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient Characteristics

A total of 142 patients with severe MR after TEER were identified and included in the analysis (Figure 1). Most patients (86%) had recurrent (versus persistent) MR. Among the 142 included patients, 44 (31.0%) underwent mitral valve surgery and 98 (69.0%) were managed medically. Patients who underwent surgery were younger than those treated medically (74.1 \pm 8.9 versus 78.6 \pm 10.5 years, *P*=0.01). The prevalence of major comorbidities was similar in both group except



Figure 1. Study flow chart. MVR indicates mitral valve replacement.

obesity and sleep apnea, which were more prevalent in the surgical group (Table 1). The Society of Thoracic Surgeons Predicted Risk of Operative Mortality at the time of severe MR diagnosis (index procedure in patients with persistent MR and at time of first echo showing severe MR in patients with recurrent MR) was similar in the 2 groups (9.0±4.7 versus 7.9±4.9 in the surgical versus medical therapy groups, respectively, P=0.22).

Transcatheter Edge to Edge Repair

Index TEER indications and procedural outcomes were comparable between in the surgical versus medical therapy groups, as shown in Table 2. This included severe primary MR (52.3% versus 53.1%), secondary MR

Table 1.	Baseline Characteristics at the Time of Recurrent
MR Deteo	ction

Baseline characteristics	Mitral surgery (N=44)	Medical therapy (N=98)	P value
Age, y	74.1±8.9	78.6±10.5	0.01
Male sex, n (%)	30 (68.2)	70 (71.4)	0.70
White race, n (%)	44 (100.0)	93 (94.9)	0.32
Body mass index, kg/m ²	28.9±5.9	26.8±4.9	0.03
Smoking, n (%)	27 (61.4)	51 (52.0)	0.30
Hypertension, n (%)	38 (86.4)	83 (84.7)	0.80
Dyslipidemia, n (%)	31 (70.5)	70 (71.4)	0.91
Diabetes, n (%)	14 (31.8)	28 (28.6)	0.67
Known coronary artery disease, n (%)	28 (63.6)	57 (58.2)	0.54
Prior myocardial infraction, n (%)	9 (20.5)	27 (27.6)	0.37
Prior percutaneous coronary intervention, n (%)	14 (31.8)	31 (31.6)	0.98
Coronary artery bypass grafting, n (%)	14 (31.8)	32 (32.7)	0.92
Prior sternotomy, n (%)	21 (47.7)	35 (35.7)	0.18
STS risk of operative mortality, n (%)*	9.0±4.7	7.9±4.9	0.22
Peripheral arterial disease, n (%)	6 (13.6)	19 (19.4)	0.41
Prior transient ischemic attack/ stroke, n (%)	10 (22.7)	12 (12.2)	0.11
Obstructive sleep apnea, n (%)	23 (52.3)	33 (33.7)	0.04
End stage renal disease, n (%)	2 (4.5)	4 (4.1)	0.99
Pacemaker, n (%)	7 (15.9)	25 (25.5)	0.20
Chronic lung disease, n (%)	12 (27.3)	27 (27.6)	0.97
Congestive heart failure, n (%)	37 (84.1)	87 (88.8)	0.44
NYHA III, n (%)	30 (68.2)	60 (61.2)	0.43
NYHA IV, n (%)	6 (13.6)	19 (19.4)	0.40
Atrial fibrillation, n (%)	26 (59.1)	62 (63.3)	0.64
Paroxysmal, n (%)	7 (15.9)	22 (22.4)	0.37
Permanent, n (%)	17 (38.6)	40 (40.8)	0.81

MR indicates mitral regurgitation; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

*STS at the time of recurrent MR.

(13.6% versus 14.3%), and mixed etiology MR (34.1% versus 32.6%) in the surgical versus medical groups respectively. One MitraClip was implanted in 59.2% versus 50.0% of patients, and 2 clips were implanted in 40.8% versus 50.0% of patients in the surgery and medical management groups, respectively. Successful MR reduction to ≤Moderate (81.8% versus 87.8%) and mitral gradient (4.6±2.2 versus 4.0±1.8mmHg) were also similar in the 2 groups. The percentage of failed cases per year was defined as patients presenting with moderate to severe or severe MR. During the initial experience in 2014, the failure rate was 30%. Yet, in the past 2 years, it was only 20% and 5%, respectively (Figure 2).

Echocardiographic Characteristics

The time from the index TEER procedure to detection of severe recurrent MR was similar in both groups (mean±SD 230±331 versus 285±380 davs. median [interguartile range] 97.5 [39.5-384] versus 93.5 [40-389] days in the surgical versus medical groups, respectively [P>0.05]) (Figure 3). There were several differences in the echocardiographic parameters at the time of recurrent MR detection. Patients in the surgical group had a higher mean LV ejection fraction (58.1±9.7% versus 47.1±15.8%, P<0.001) compared with patients treated medically. They also had smaller LV dimensions but similar right ventricular systolic pressure and a similar prevalence of ≥moderate tricuspid regurgitation. (Table 3). Three types of recurrent MR mechanisms were seen at follow-up. Single leaflet device attachment (22.2% versus 2.3%, P < 0.001) was more prevalent in the surgical group as compared with the medical group, but similar rates of

Table 2.	Index TEER Procedure Characteristics
----------	--------------------------------------

TEER procedure details	Mitral surgery (N=44)	Medical therapy (N=98)	P value	
Etiology of MR				
Primary, n (%)	23 (52.3)	52 (53.1)	0.93	
Secondary, n (%)	6 (13.6)	14 (14.3)	0.92	
Mixed primary/secondary, n (%)	15 (34.1)	32 (32.6)	0.87	
Number of TEER devices				
1 clip implanted, n (%)	26 (59.2)	49 (50.0)	0.32	
2 clips implanted, n (%)	18 (40.8)	49 (50.0)	0.32	
Post-TEER deployment				
≤Moderate MR, n (%)	36 (81.8)	86 (87.8)	0.35	
Mitral gradient, mmHg	4.6±2.2	4.0±1.8	0.13	
Tricuspid regurgitation				
Moderate, n (%)	10 (22.7)	23 (23.4)	0.92	
Severe, n (%)	6 (13.6)	20 (20.4)	0.33	

MR indicates mitral regurgitation; and TEER, transcatheter edge-to-edge repair.

progressive worsening MR of the previously treated zone (66.6% versus 77.9%, P=0.25) and new leaflet pathology (11.1% versus 19.7%, P=0.30) were observed, as shown in Figure 4.

Operative Characteristics and Outcomes

The time interval between detection of recurrent MR and mitral valve surgery is shown in Figure 5. Among the 44 patients who underwent mitral valve surgery for recurrent MR, 4 had concurrent severe mitral stenosis. Six patients with functional MR underwent surgery because of a concomitant indication including tricuspid repair, tricuspid annuloplasty, ligation of the left atrial appendage, or coronary artery bypass graft. In addition, 12 patients underwent the index TEER procedure at other institutions. Surgeries were performed through a median sternotomy in 40 patients, and through right thoracotomy in 4 patients. Mitral valve replacement was required in all patients, with most patients (79.6%) receiving a tissue prosthesis. Atraumatic clip removal was feasible in 8 (18.2%) patients with single leaflet device attachment. However, significant fibrosis preventing atraumatic clip removal was noted in 34 (81.8%) of patients. This required partial resection of the fibrotic valvular tissue surrounding the clip but the subvalvular apparatus was preserved. Atrial septostomy closure was performed in all 44 patients, and most patients underwent at least 1 concomitant procedure (Table 4). Median aortic cross-clamp and bypass time was 85.0 (58.0-106.5) and 131.5 (98.2-160.2) minutes, respectively. The median duration of mechanical ventilation was 9.2 (4.0-51.0) hours; the median duration of intensive care stay was 66 (24.0-139.7) hours; the median length of hospital stay was 10.6 (7.0-22.5) days. Operative mortality occurred in 2 patients (4.5%; observed/expected operative mortality ratio=0.55). Postoperative complications were uncommon as shown in Table 5.



Figure 2. The percentage of failed cases per year.



Figure 3. Time interval between index edge-to-edge procedure and detection of severe recurrent mitral regurgitation.

Comparative Analysis of Mitral Surgery Versus Medical Therapy

Median follow-up duration was 871 (interquartile range 479–1684) versus 434 (interquartile range

Table 3.	Echocardiographic Parameters at the Time of
First Det	ected Recurrent MR

First echocardiogram with recurrent MR	Mitral surgery (N=44)	Medical therapy (N=98)	P value	
Days to recurrent MR	230.3±330.7	285.1±379.6	0.38	
LV ejection fraction, (%)	58.1±9.7	47.1±15.8	<0.001	
Heart rate, bpm	71.3±14.2	73.6±12.5	0.43	
Mitral gradient, mmHg	5.6±3.0	4.9±2.5	0.17	
LV end-systolic diameter, mm	36.3±6.0	42.2±11.8	0.001	
LV end-diastolic diameter, mm	53.0±4.7	56.9±9.1	0.004	
Right ventricular systolic pressure, mmHg	55.0±12.1	52.5±12.9	0.35	
Mitral annular calcification, n (%)	11 (25)	44 (44.9)	0.02	
Severity of tricuspid regurgitation				
≥Moderate, n (%)	23 (52.3)	54 (55.1)	0.75	
Moderate, n (%)	14 (31.8)	30 (30.6)	0.89	
Severe, n (%)	9 (20.5)	24 (24.5)	0.60	

LV indicates left ventricular; and MR, mitral regurgitation.

186–829) days for the surgical versus medical therapy groups, respectively (P<0.001). During follow-up, a total of 50 patients died: 15 in the surgical group and 35 in the medical treatment arm. Kaplan–Meier analysis showed a significantly lower mortality in the surgical group (log-rank P=0.0014) (Figure 6). In the Cox model, after adjusting for age, body mass index, LV ejection fraction, and LV dimensions, mitral valve surgery was associated with significantly lower all-cause mortality (adjusted HR,



Figure 4. Mechanism of severe recurrent mitral regurgitation in the medical therapy and mitral valve surgery groups.

SLDA indicates single leaflet device attachment.



Figure 5. Time interval between detection of severe recurrent mitral regurgitation and mitral valve surgery in the surgical cohort.

0.36 [95% Cl, 0.15–0.85], *P*=0.02) (Table 6). A secondary analysis including only patients with recurrent MR (n=122) revealed similar findings (adjusted

Operative characteristics	Mitral surgery
Median sternotomy, n (%)	40 (90.9)
Right thoracotomy approach, n (%)	4 (9.1)
Mitral valve surgery	
Mitral valve replacement, n (%)	44 (100)
Mechanical, n (%)	9 (20.4)
Tissue, n (%)	35 (79.6)
Associated cardiac procedures	
Atrial septostomy closure, n (%)	44 (100)
Coronary artery bypass grafting, n (%)	9 (20.4)
Tricuspid valve surgery, n (%)	19 (43.2)
Exclusion of left atrial appendage, n (%)	4 (9.1)
Maze procedure, n (%)	2 (4.5)
Aortic surgery, n (%)	2 (4.5)
Aortic cross-clamp time, min	85.0 (58.0–106.5)
Cardiopulmonary bypass time, min	131.5 (98.2–160.2)
Intraoperative transfusions	
Red blood cell transfusion, n (%)	23 (52.3)
Platelet transfusion, n (%)	27 (61.4)
Fresh frozen plasma transfusion, n (%)	21 (47.7)
Cryoprecipitate transfusion, n (%)	4 (9.1)

Table 4.	Operative	Characteristics
	operative	onaracteristics

HR, 0.24 [95% CI, 0.09–0.69], P=0.008) (Figure 7 and Table 7). Moreover, the rate of rehospitalization for heart failure was 14.3% in the medical group as compared with 9.1% in the surgery group. The survival analysis demonstrated a significantly higher incidence of readmission for heart failure (log-rank P=0.02) (Figure 8).

Table 5. Operative Outcomes After Mitral Valve Surgery

Operative outcomes	Mitral surgery
Operative mortality, n (%)	2 (4.5)
Length of mechanical ventilation, h (IQR)	9.2 (4.0–51.0)
Intensive care unit length of stay, h (IQR)	66.0 (24.0–139.7)
Hospital length of stay, d (IQR)	10.6 (7.0–22.5)
Postoperative atrial fibrillation, n (%)	15 (34.1)
Pneumonia, n (%)	9 (20.4)
Renal failure, n (%)	10 (22.7)
Delayed sternal closure, n (%)	5 (11.3)
Gastrointestinal bleeding, n (%)	4 (13.6)
Intra-aortic balloon pump use, n (%)	4 (9.1)
Sepsis, n (%)	2 (4.5)
Extracorporeal membrane oxygenation use, n (%)	2 (4.5)
Reexploration for surgical bleeding, n (%)	1 (0.3)
Stroke, n (%)	1 (0.3)

IQR indicates interquartile range.



Figure 6. Kaplan-Meier survival curves for all-cause mortality in patients with severe persistent or recurrent mitral regurgitation after TEER stratified by treatment strategy.

TEER indicates transcatheter edge-to-edge repair.

DISCUSSION

This study documents 2 novel findings: (1) mitral surgery for persistent or recurrent severe MR after TEER at experienced mitral centers can be performed with favorable outcomes; and (2) compared with medical therapy, surgery is associated with a substantial reduction in all-cause mortality during midterm followup. These findings deserve further elaboration.

Mitral TEER has become a popular treatment option for selected patients with severe symptomatic MR with \approx 10000 cases performed in 2019. The volume trends with TEER are expected to further grow considerably with the publication of the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial and the new American College of Cardiology/American Heart Association guidelines assigning TEER a class IIa indication for persistent severe functional MR despite optimal medical therapy.^{1,13–15} Despite its proven efficacy as an alternative to surgery in high-risk patients, recurrent MR has been a concern with TEER with up to 15% of patients reported to have significant recurrent MR during midterm follow-up.^{2,4,5}

Table 6	Multivariate Cox Reg	ression Analysis f	or Prediction of	All-Cause Mortality
Table 0.	wullivariate out neg	ression Analysis i	OF FIEURCHOIL OF	All-Cause with tally

	Univariate Cox model		Multivariate Cox model	
Characteristics	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.003 (0.97–1.03)	0.85	0.99 (0.95–1.03)	0.66
Body mass index	1.001 (0.95–1.05)	0.95	0.97 (0.90–1.05)	0.44
Obstructive sleep apnea	1.24 (0.71–2.18)	0.44	1.93 (0.85–4.37)	0.11
LV ejection fraction	0.98 (0.96–1.002)	0.07	1.02 (0.97–1.06)	0.46
LV end-systolic diameter	1.01 (0.98–1.04)	0.40	1.01 (0.92–1.12)	0.79
LV end-diastolic diameter	1.01 (0.97–1.05)	0.53	1.01 (0.92–1.12)	0.94
Mitral valve surgery	0.36 (0.19–0.69)	0.002	0.36 (0.15–0.85)	0.02

HR indicates hazard ratio; and LV, left ventricular.



Figure 7. Kaplan–Meier survival curves for all-cause mortality in patients with severe recurrent mitral regurgitation after TEER stratified by treatment strategy.

TEER indicates transcatheter edge-to-edge repair.

With the growing volume and the expected expansion of TEER to the large potential pool of patients with functional MR and to lower risk patients (with higher expected longevity), the emergence of a sizable cohort of patients with recurrent MR is conceivable.

Addressing severe MR after TEER requires a multifaceted approach that starts with careful patient selection by the heart team, referral of complex anatomies to high-volume centers, and improvement in procedural planning. Nonetheless, even with applying the best mitigation strategies, it is expected that a number of patients will present with recurrent MR and worsening symptoms. The management of these patients represent a conundrum. Transcatheter

Table 7.Multivariate Cox Regression Analysis for Prediction of All-Cause Mortality in Patients With Recurrent MitralRegurgitation

	Univariate Cox model		Multivariate Cox model	Multivariate Cox model	
Characteristics	HR (95% CI)	P value	HR (95% CI)	P value	
Age	1.01 (0.97–1.04)	0.48	0.99 (0.95–1.03)	0.58	
Body mass index	0.99 (0.94–1.05)	0.86	0.99 (0.91–1.07)	0.79	
Obstructive sleep apnea	1.15 (0.62–2.13)	0.65	1.57 (0.65–3.82)	0.32	
LV ejection fraction	0.98 (0.96–1.005)	0.12	1.02 (0.97–1.07)	0.50	
LV end-systolic diameter	1.007 (0.97–1.03)	0.64	0.99 (0.90–1.10)	0.92	
LV end-diastolic diameter	1.004 (0.96–1.04)	0.84	1.01 (0.92–1.11)	0.81	
Mitral valve surgery	0.23 (0.10–0.51)	<0.001	0.24 (0.09–0.69)	0.008	

HR indicates hazard ratio; and LV, left ventricular.



Figure 8. Kaplan–Meier survival curves for heart failure readmission in patients with severe recurrent mitral regurgitation after TEER stratified by treatment strategy.

TEER indicates transcatheter edge-to-edge repair.

intervention with redo TEER is often limited by anatomical constraints (residual gradient, small annulus, limited tissue for leaflet insertion and grasping, etc).^{16,17} Use of transcatheter electrosurgical techniques to sever the tissue bridge created by TEER, followed by transcatheter mitral valve implantation, has been described in a small case series but is still in the experimental stage.¹⁸ Mitral valve surgery is also hindered by the high-risk clinical profile and the higher observed than expected mortality with surgery after TEER recently reported.^{12,19} Hence, the optimal management of patients with recurrent MR after TEER remains an open question.

Data from the Society of Thoracic Surgeons registry showed worse than expected outcomes with surgery after failed TEER but included a large number (n=227) of centers with heterogenous experiences. In a secondary volume-outcomes analysis, observed-toexpected mortality was much better in high- versus low-volume centers, which is in line with our findings.¹² However, the novelty in our study is its inclusion of a risk-adjusted comparative outcomes analysis of surgery versus medical therapy. This analysis showed that patients with recurrent severe MR after TEER who undergo surgery have \approx 65% lower risk-adjusted mortality compared with those treated medically. These findings suggest that referral to mitral surgery at an experienced center after failed TEER may be the optimal management approach in these patients.

Limitations

Our study has several limitations. First, this is a retrospective, single-center study and hence is hindered by the inherent limitations of observational studies. Second, the study included patients who had TEER at our centers and at other centers. Hence, it is not possible to accurately estimate the proportion of patients with recurrent MR after TEER. However, this has been reported before and it was not the main objective of the study. Third, despite the comparable baseline risk profile between the 2 groups and our adjustment for the different characteristics using logistic regression, the impact of selection bias cannot be eliminated. Reasons for not undergoing surgery in the medical arm included patient or referring provider preference, the perceived high morbidity and mortality with the operation, and other factors that could not be quantified in this study. Nonetheless, it is unlikely that randomized data on the management of recurrent MR after TEER will become available. Hence, despite this limitation, the findings of this study remain informative and relevant to current practice.

CONCLUSIONS

Surgical treatment of severe MR after mitral TEER is feasible but requires mitral valve replacement. Compared with medical therapy, mitral surgery is associated with significantly lower risk-adjusted all-cause mortality during midterm follow-up.

ARTICLE INFORMATION

Received March 29, 2022; accepted July 21, 2022.

Affiliations

Department of Cardiovascular Disease (A.E.S., A.C.P., M.G., C.S.R., M.A.) and Department of Cardiovascular Surgery (P.M., K.G., A.A., M.F.E., J.A.C.), Mayo Clinic, Rochester, MN.

Sources of Funding

None.

Disclosures

None.

REFERENCES

- Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP III, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e35–e71. doi: 10.1161/CIR.000000000000932
- Mack M, Carroll JD, Thourani V, Vemulapalli S, Squiers J, Manandhar P, Deeb GM, Batchelor W, Herrmann HC, Cohen DJ, et al. Transcatheter mitral valve therapy in the United States: a report from the STS/ACC TVT Registry. *Ann Thorac Surg.* 2022;113:337–365. doi: 10.1016/j. athoracsur.2021.07.030
- Alkhouli M, Sulaiman S, Osman M, El Shaer A, Mayahni AA, Kawsara A. Trends in outcomes, cost, and readmissions of transcatheter edge to edge repair in the United States (2014–2018). *Catheter Cardiovasc Interv*. 2022;99:949–955. doi: 10.1002/ccd.29957
- Ailawadi G, Lim DS, Mack MJ, Trento A, Kar S, Grayburn PA, Glower DD, Wang A, Foster E, Qasim A, et al. One-year outcomes after MitraClip for functional mitral regurgitation. *Circulation*. 2019;139:37–47. doi: 10.1161/ CIRCULATIONAHA.117.031733
- Nickenig G, Estevez-Loureiro R, Franzen O, Tamburino C, Vanderheyden M, Lüscher TF, Moat N, Price S, Dall'Ara G, Winter R, et al. Percutaneous mitral valve edge-to-edge repair: in-hospital results and 1-year follow-up of 628 patients of the 2011–2012 Pilot European Sentinel Registry. J Am Coll Cardiol. 2014;64:875–884. doi: 10.1016/j. jacc.2014.06.1166
- Sugiura A, Kavsur R, Spieker M, Iliadis C, Goto T, Ozturk C, Weber M, Tabata N, Zimmer S, Sinning JM, et al. Recurrent mitral regurgitation

after MitraClip: predictive factors, morphology, and clinical implication. *Circ Cardiovasc Interv.* 2022;15:e010895.

- Hassan A, Eleid MF. Recurrent mitral regurgitation after MitraClip: defining success and predicting outcomes. *Circ Cardiovasc Interv.* 2022;15:e011837. doi: 10.1161/CIRCINTERVENTIONS.122.011837
- Kaneko H, Neuss M, Weissenborn J, Butter C. Impact of residual mitral regurgitation after MitraClip implantation. *Int J Cardiol.* 2017;227:813– 819. doi: 10.1016/j.ijcard.2016.10.054
- Buzzatti N, De Bonis M, Denti P, Barili F, Schiavi D, Di Giannuario G, La Canna G, Alfieri O. What is a "good" result after transcatheter mitral repair? Impact of 2+ residual mitral regurgitation. *J Thorac Cardiovasc Surg.* 2016;151:88–96. doi: 10.1016/j.jtcvs.2015.09.099
- Paranskaya L, D'Ancona G, Bozdag-Turan I, Akin I, Kische S, Turan GR, Rehders T, Ortak J, Nienaber CA, Ince H. Residual mitral valve regurgitation after percutaneous mitral valve repair with the MitraClip(R) system is a risk factor for adverse one-year outcome. *Catheter Cardiovasc Interv*. 2013;81:609–617. doi: 10.1002/ccd.24586
- Reichart D, Kalbacher D, Rubsamen N, Tigges E, Thomas C, Schirmer J, Reichenspurner H, Blankenberg S, Conradi L, Schafer U, et al. The impact of residual mitral regurgitation after MitraClip therapy in functional mitral regurgitation. *Eur J Heart Fail*. 2020;22:1840–1848. doi: 10.1002/ejhf.1774
- Chikwe J, O'Gara P, Fremes S, Sundt TM III, Habib RH, Gammie J, Gaudino M, Badhwar V, Gillinov M, Acker M, et al. Mitral surgery after transcatheter edge-to-edge repair: Society of Thoracic Surgeons Database analysis. J Am Coll Cardiol. 2021;78:1–9. doi: 10.1016/j.jacc.2021.04.062
- Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, et al. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med. 2018;379:2307–2318. doi: 10.1056/NEJMoa1806640
- Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med.* 2011;364:1395–1406. doi: 10.1056/NEJMoa1009355
- Asch FM, Grayburn PA, Siegel RJ, Kar S, Lim DS, Zaroff JG, Mishell JM, Whisenant B, Mack MJ, Lindenfeld J, et al. Echocardiographic outcomes after transcatheter leaflet approximation in patients with secondary mitral regurgitation: the COAPT trial. J Am Coll Cardiol. 2019;74:2969–2979. doi: 10.1016/j.jacc.2019.09.017
- Sugiura A, Weber M, Tabata N, Goto T, Ozturk C, Hammerstingl C, Sinning JM, Werner N, Nickenig G. Prognostic impact of redo transcatheter mitral valve repair for recurrent mitral regurgitation. *Am J Cardiol.* 2020;130:123–129. doi: 10.1016/j.amjcard.2020.06.025
- Kreidel F, Frerker C, Schlüter M, Alessandrini H, Thielsen T, Geidel S, Schäfer U, Kuck KH. Repeat MitraClip therapy for significant recurrent mitral regurgitation in high surgical risk patients: impact of loss of leaflet insertion. *JACC Cardiovasc Interv.* 2015;8:1480–1489. doi: 10.1016/j. jcin.2015.06.019
- Lisko JC, Greenbaum AB, Guyton RA, Kamioka N, Grubb KJ, Gleason PT, Byku I, Condado JF, Jadue A, Paone G, et al. Electrosurgical detachment of MitraClips from the anterior mitral leaflet prior to transcatheter mitral valve implantation. *JACC Cardiovasc Interv.* 2020;13:2361–2370. doi: 10.1016/j.jcin.2020.06.047
- Kreidel F, Alessandrini H, Wohlmuth P, Schmoeckel M, Geidel S. Is surgical or catheter-based interventions an option after an unsuccessful mitral clip? *Semin Thorac Cardiovasc Surg.* 2018;30:152–157. doi: 10.1053/j.semtcvs.2018.03.005