Journal of the American Heart Association

ORIGINAL RESEARCH

MitraClip After Failed Surgical Mitral Valve Repair—An International Multicenter Study

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BACKGROUND: Recurrence of mitral regurgitation (MR) after surgical mitral valve repair (SMVR) varies and may require reoperation. Redo mitral valve surgery can be technically challenging and is associated with increased risk of mortality and morbidity. We aimed to assess the feasibility and safety of MitraClip as a treatment strategy after failed SMVR and identify procedure modifications to overcome technical challenges.

METHODS AND RESULTS: This international multicenter observational retrospective study collected information for all patients from 16 high-volume hospitals who were treated with MitraClip after failed SMVR from October 29, 2009, until August 1, 2017. Data were anonymously collected. Technical and device success were recorded per modified Mitral Valve Academic Research Consortium criteria. Overall, 104 consecutive patients were included. Median Society of Thoracic Surgeons score was 4.5% and median age was 73 years. At baseline, the majority of patients (82%) were in New York Heart Association class ≥III and MR was moderate or higher in 86% of patients. The cause of MR pre-SMVR was degenerative in 50%, functional in 35%, mixed in 8%, and missing/unknown in 8% of patients. The median time between SMVR and MitraClip was 5.3 (1.9–9.7) years. Technical and device success were 90% and 89%, respectively. Additional/modified imaging was applied in 21% of cases. An MR reduction of ≥1 grade was achieved in 94% of patients and residual MR was moderate or less in 90% of patients. In-hospital all-cause mortality was 2%, and 86% of patients were in New York Heart Association class ≤II.

CONCLUSIONS: MitraClip is a safe and less invasive treatment option for patients with recurrent MR after failed SMVR. Additional/modified imaging may help overcome technical challenges during leaflet grasping.

Key Words: MitraClip ■ recurrent mitral regurgitation ■ surgical mitral valve repair

See Editorial by Glower

Mitral valve surgery is the treatment of choice for symptomatic patients with severe degenerative mitral regurgitation (MR) and left ventricular (LV) ejection fraction >30%.[1,2] In functional MR, surgery is indicated in patients with severe MR undergoing coronary artery bypass grafting and LV ejection fraction >30%.[2] Recurrence of MR after surgical repair varies and may require reoperation.[3–5] Compared with primary mitral surgery, redo mitral valve surgery can be technically challenging and is associated with a higher operative mortality, higher complication rate, and increased length of stay.[6] Alternatively, transcatheter mitral valve replacement and percutaneous mitral valve edge-to-edge repair

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Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.019236

For Sources of Funding and Disclosures, see page 10.

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

CLINICAL PERSPECTIVE

What Is New?

- MitraClip after failed surgical mitral valve repair is feasible and safe in selected patients, with a technical and device success rate of 90% and 89%, respectively.
- Procedure modifications may be required to overcome technical challenges related to prior mitral surgery.

What Are the Clinical Implications?

- For selected patients with recurrent mitral regurgitation after failed surgical mitral valve repair, MitraClip is a safe and less invasive treatment option.
- Additional/modified imaging may help overcome technical challenges during leaflet grasping.

Nonstandard Abbreviations and Acronyms

CTSN	Cardiothoracic Surgical Trials Network
EVEREST II	Endovascular Valve Edge-to-Edge Repair Study II
MR	mitral regurgitation
MVARC	Mitral Valve Academic Research Consortium
SMVR	surgical mitral valve repair
STS	Society of Thoracic Surgeons

with MitraClip can be performed in selected patients after failed surgical mitral valve repair (SMVR).[7–11] The aim of this study was to assess the feasibility and safety of MitraClip after failed SMVR and identify procedure modifications to overcome technical challenges related to the prior mitral surgery.

METHODS

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

This international multicenter observational retrospective study collected information from all consecutive patients, from 16 high-volume hospitals, who were treated with MitraClip after failed SMVR from October 29, 2009, until August 1, 2017. Selection of patients and assessment of eligibility was left at the discretion of the local multidisciplinary heart teams, which included interventional cardiologists, imaging specialists, and cardiac surgeons. Data were anonymously collected.

The medical ethics committee of the Erasmus Medical Center reviewed the study protocol and waived the need for additional informed consent because of the noninterventional design of this retrospective study (MEC-2017-1021) using anonymous data collection. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Study End Points and Definitions

The primary end points were procedural safety expressed as "technical success" and procedural efficacy expressed as "device success," both were modified from Mitral Valve Academic Research Consortium (MVARC) criteria.[12]

1. Technical success is defined as successful deployment of the device with absence of procedural mortality and freedom from emergency surgery.
2. Device success is defined as proper placement of the device without procedural mortality and with reduction in postprocedural MR by ≥1 grade from baseline and to an absolute level of moderate or higher MR.
3. Significant MR reduction is defined as reduction in postprocedural MR by ≥1 grade from baseline.
4. Device time is defined as the time from guide catheter insertion to guide catheter removal.

Statistical Analysis

Categorical variables are presented as frequencies and percentages and compared using Pearson chi-square test or Fisher exact test, as appropriate. Continuous variables are presented as means (±SD) (in case of normal distribution) or medians (interquartile range) (in case of skewed distribution) and compared with using Student *t* test or Mann Whitney *U* test. Normality of the distributions was assessed using the Shapiro-Wilk test. A 2-sided α level of 0.05 was used to indicate significance. Statistical analyses were performed using SPSS software version 21.0 (IBM).

RESULTS

Baseline Characteristics

Overall, 104 consecutive patients were included with a median age of 73 years, 70% were men, 82% were in New York Heart Association class ≥III, and the median Society of Thoracic Surgeons (STS) score was 4.5% (Table 1). The median LV ejection fraction was 50% (30%–60%), mean LV end-diastolic diameter was 60±11 mm, and transmitral gradient was 3.0 mm Hg

(interquartile range, 2.2–4.0 mm Hg) (Table 1). The cause of MR pre-SMVR was degenerative in 50%, functional in 35%, mixed in 8%, and missing/unknown in 8%, and further specified in Table 2. The cause of MR pre-MitraClip was degenerative in 44%, functional in 39%, mixed in 10%, ring rupture/detachment/dehiscence in 7%, and systolic anterior motion in 3% (Table 2 and Figure 1A). The median time between surgery and MitraClip was 5.3 years (Table 2).

Table 1. Baseline Characteristics

	Total Population (N=104)
Age, median (IQR), y	73.0 (67.0–80.0)
Men, n (%)	73 (70)
Height, mean±SD, cm	171±10
Weight, median (IQR), kg	75.0 (65.0–85.0)
BMI, median (IQR), kg/m^2	24.9 (22.7–28.0)
NYHA class ≥III, n (%)	85 (82)
STS score, median (IQR), %	4.5 (2.2–6.6)
Cardiomyopathy, n (%)	
Ischemic	32 (36)
Nonischemic	12 (13)
Hypertrophic	1 (1)
Implantable device, n (%)	
Permanent pacemaker	9 (9)
ICD	16 (15)
CRT	11 (11)
Atrial fibrillation, n (%)	
Paroxysmal	30 (29)
Permanent	30 (29)
Previous myocardial infarction	27 (27)
Previous coronary artery bypass graft surgery	38 (37)
Previous percutaneous coronary intervention	20 (19)
Previous cerebrovascular event	7 (7)
Diabetes mellitus	24 (23)
Hypertension	82 (79)
Peripheral vascular disease	13 (13)
Pulmonary hypertension	65 (63)
Chronic obstructive pulmonary disease	20 (19)
Laboratory results	
GFR, mean±SD, mL/min	56±21
Hemoglobin, median (IQR), mmol/L	6.6 (7.9–8.6)
Echocardiography	
LV ejection fraction, median (IQR), %	50 (30–60)
LV end-diastolic diameter, mean±SD, mm	60±11
LV end-systolic diameter, mean±SD, mm	45±13
Mean transmitral gradient, median (IQR), mm Hg	3.0 (2.2–4.0)
Severity mitral regurgitation	
Mild-moderate, n (%)	3 (3)
Moderate, n (%)	12 (12)
Moderate-severe, n (%)	37 (36)
Severe, n (%)	52 (50)

BMI indicates body mass index; CRT, cardiac resynchronization therapy; GFR, glomerular filtration rate; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LV, left ventricular; NYHA, New York Heart Association; and STS, Society of Thoracic Surgeons.

Procedural Characteristics

MitraClip implantation was feasible in 92% of patients. In the unfeasible cases (8%), reasons for not clipping were development of inacceptable mitral valve gradients in 5 cases, persistent MR in combination with inacceptable mitral valve gradient in 1 case, and inability to grasp both leaflets because of a severely tethered and short posterior leaflet in combination with poor image quality in 2 cases. Seven of

Table 2. Mitral Valve Regurgitation Cause, Treatment, and Mode of Failure

	Total Population (N=104)
Cause MR before surgical repair	
Degenerative MR, n (%)	52 (50)
Prolapse, n (%)	32 (62)
Chordal rupture, n (%)	7 (14)
Other, n (%)	6 (12)
Functional MR, n (%)	36 (35)
Annular dilatation, n (%)	11 (31)
Leaflet tethering, n (%)	13 (36)
Both, n (%)	9 (25)
Mixed, n (%)	8 (8)
Missing/unknown, n (%)	8 (8)
Type of surgical mitral valve repair	
Ring, n (%)	90 (87)
Chordal repair, n (%)	13 (13)
Partial leaflet resection, n (%)	16 (15)
Other, n (%)	8 (8)
Combined (ring/chordal repair/resection), n (%)	28 (27)
Type of ring	
Complete ring, n (%)	65 (70)
Incomplete ring, n (%)	25 (28)
Ring size, mm	
25–30	37 (41)
31–35	26 (29)
36–40	11 (12)
Cause pre-MitraClip	
Degenerative, n (%)	46 (44)
Functional, n (%)	41 (39)
Mixed, n (%)	10 (10)
Ring rupture/detachment, n (%)	7 (7)
Systolic anterior motion, n (%)	3 (3)
Median time (IQR) between surgery and MitraClip, y	5.3 (1.9–9.7)

IQR indicates interquartile range; and MR, mitral regurgitation.

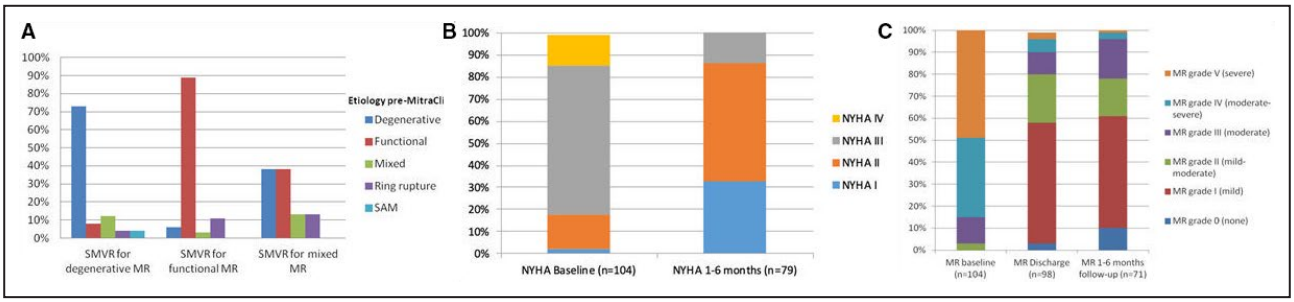

Figure 1. Baseline characteristics (eg, mitral regurgitation [MR] etiology) and follow-up of New York Heart Association (NYHA) class and MR.
A, Overview of MR etiologies before surgical mitral valve repair (SMVR) and before MitraClip procedure. **B**, NYHA at baseline and at 1 to 6 months of follow-up. **C**, MR at baseline, at discharge, and at 1 to 6 months of follow-up. SAM indicates systolic anterior motion.

the 8 patients (the unfeasible cases) had a surgical annuloplasty ring, 2 patients had a 28-mm size ring, 3 patients had a 30-mm size ring, 1 patient had a 32-mm size ring, and the ring size was missing in 1 patient. Overall, 64% of patients were treated with 1 clip, 23% with 2 clips, and 5% with 3 clips. Significant MR reduction (MR reduction ≥1 grade) and technical and device success were achieved in 94%, 90%, and 89%, respectively. There was no difference in technical and device success between patients treated with degenerative versus functional MR pre-SMVR (89% versus 97% [*P*=0.23] and 88% versus 94% [*P*=0.46], respectively) (Table 3).

In 79% of the patients, standard transesophageal echocardiography (TEE) views (ie, LV outflow tract and intercommisural view) were used during the grasping process, in 16% of the patients transesophageal echocardiography views were used with modified angles, and in 5% of the patients standard transesophageal echocardiography views were used in combination with adjunctive intracardiac echocardiography.

The median device time was 70 minutes and appeared shorter with additional/modified imaging versus standard LV outflow tract/intercommissural view (39 minutes [21–67 minutes] versus 79 minutes [56–116 minutes], *P*<0.001). However, there was no difference between the 2 groups (standard views versus additional/modified imaging) with regards to technical success (89% versus 95%, *P*=0.68) and device success (87% versus 95%, *P*=0.45).

In-Hospital Complications and Follow-Up

The in-hospital mortality rate was 2% and a similar percentage was seen for major bleeding and minor vascular complication. Minor bleeding occurred in 3% of patients. The median length of stay was 3 days. New York Heart Association class and MR at 1 month to 6 months are shown in Figure 1B and 1C. Mortality rates at 6 months and 1 year were 6% and 9%, respectively.

DISCUSSION

We report the largest series of patients treated with MitraClip after failed SMVR. The findings indicate that: (1) MitraClip was feasible and safe after failed SMVR in selected patients with technical and device success rates of 90% and 89%, respectively; (2) the median time between SMVR and MitraClip was 5.3 years; and (3) additional/modified imaging techniques may facilitate leaflet grasping and shorten device time by dealing with technical challenges caused by shadowing from the annuloplasty ring (Figure 2).

Recurrence of MR after SMVR is not uncommon and is associated with an increased risk of mortality.[13,14] Petrus et al[13] demonstrated that the cumulative incidence of recurrent MR (grade ≥2) after SMVR for functional ischemic MR is 27.6% (at 10 years of follow-up). One of the randomized CTSN (Cardiothoracic Surgical Trials Network) initiatives compared mitral repair with mitral valve replacement for severe functional MR and reported MR recurrence rates of 32.6% at 1 year and 58.8% at 2 years of follow-up including mortality rates of 14.3% at 1 year and 19% at 2 years of follow-up after mitral repair.[3,15] Another CTSN trial reported an 11.2% MR recurrence 2 years after mitral repair in patients with at least moderate ischemic MR who underwent SMVR in combination with coronary artery bypass grafting.[16] EVEREST II (Endovascular Valve Edge-to-Edge Repair Study II), which was predominantly composed of degenerative causes, compared MitraClip with mitral surgery (86% surgical repair), and ≈11% of the surgical arm had moderate to severe or severe MR at 5-year follow-up.[17] Suri et al[18] showed a 15-year overall incidence rate of recurrent MR after SMVR for degenerative MR of 13.3%, while the 15-year incidence rate of mitral reoperation was 6.9%, suggesting that a substantial proportion (6.4%) of patients did not undergo redo mitral valve surgery. Compared with primary mitral surgery, redo mitral valve surgery is associated with higher operative mortality (11.1% versus 6.5%, *P*<0.0001), higher complication rates (such as

Table 3. Procedural Characteristics and In-Hospital Complications

	Total Population (N=104)
Imaging during grasping process	
Standard LVOT and intercommissural view	80 (79)
LVOT/intercommissural view with modified angles	15 (15)
LVOT/intercommissural view with ICE	6 (6)
Clips, n (%)	
0	8 (8)
1	67 (64)
2	24 (23)
3	5 (5)
MR reduction, n (%)	
0	6 (6)
1	10 (10)
2	18 (18)
3	37 (38)
4	27 (28)
≥1, n (%)§	92 (94)
LV ejection fraction, median (IQR), %	45 (28–56)
Mean transmitral gradient postclip, median (IQR), mm Hg	4.7 (3.0–6.0)
Concommitant mitral therapy, n (%)	
Plug/occluder implantation	2 (2)
Other	1 (1)
Device time, median (IQR), min*	70 (41–113)
Technical success, n (%)†	94 (90)
Device success, n (%)‡	88 (89)
Conversion to mitral valve surgery, n (%)	0 (0)
Bleeding, n (%)	
Minor	3 (3)
Major	2 (2)
Extensive	0 (0)
Life-threatening	0 (0)
Fatal	0 (0)
Vascular complication, n (%)	
Minor	2 (2)
Major	0 (0)
Stroke, n (%)	
Disabling	0 (0)
Nondisabling	1 (1)
Myocardial infarction, n (%)	1 (1)
In-hospital mortality, n (%)	2 (2)
Length of stay, median (IQR), d	3 (2–6)

ICE indicates intracardiac echocardiography; IQR, interquartile range; LV, left ventricular; and LVOT, left ventricular outflow tract.

*Device time is defined as the time from guided catheter insertion to guided catheter removal.

†Technical success is defined as successful deployment of the device with absence of procedural mortality and freedom from emergency surgery.

‡Device success is defined as proper placement of the device without procedural mortality and with reduction in postprocedural mitral regurgitation (MR) by ≥1 grade from baseline and to an absolute level of moderate or higher MR.

§ Reduction of the mitral regurgitation with 1 grade or more.

prolonged ventilation [28.1% versus 19.7%, $P<0.0001$], renal failure [9.4% versus 7.0%, $P=0.004$], reoperation [14.7% versus 10.3%, $P<0.0001$], stroke [2.8% versus 1.9%, $P=0.042$], cardiopulmonary bypass time [165 versus 148 minutes, $P<0.0001$], and intensive care unit stay [88 versus 68 hours, $P<0.0001$]), and increased length of stay (9 versus 7 days, $P<0.0001$).[6] In our study, using the MitraClip to treat failed SMVR was associated with a 2% in-hospital mortality rate and a short length of stay (3 days).

Our study confirms the feasibility and safety of MitraClip in patients with recurrent MR after SMVR. A previous report including 57 patients undergoing MitraClip after prior SMVR showed a procedural success rate of 84% (compared with 89% in our series).[7] In that study, patients had a higher STS score of 6.0%, a 52% functional MR pre-SMVR, and 79% of patients with original repair including a ring annuloplasty (as compared with STS 4.5%, 35% functional MR, and 87% with prior annuloplasty ring in our series).[7] However, device success in our study is still lower than what is achieved in MitraClip for native MR studies (ie, functional and/or degenerative), which varies between 91% and 96%.[19–23]

Additional/Modified Imaging and Procedure Modifications

In our study, additional/modified imaging techniques had favorable effects on device time and similar technical and device success rates. A nondehisced annuloplasty ring approximates the leaflets, minimizes the coaptation gap, and increases coaptation length, which may facilitate the grasping maneuver. Conversely, shadowing from the annuloplasty ring may obscure the echocardiographic window for posterior leaflet grasping and also limit the orifice dimensions through which the clip needs to enter the left ventricle from the left atrium. Conventional clip passing is recommended in an ≈180° open configuration to help maintain and monitor the clip orientation as the clip is positioned perpendicular to the coaptation plane before leaflet grasping. In the case of a prior surgical ring, there is a reduction in the mitral orifice such that it can sometimes be impossible to enter the left ventricle in this 180° open position, and the clip should be formally oriented in the left atrium, closed, then advanced into the left ventricle in the partially or totally closed position and reopened under the mitral plane with confirmation of the maintained correct orientation (Figure 3). The leaflets will be typically grasped well below the surgical ring and more towards the left ventricle (and more often so in secondary MR). At times, the presence of the surgical ring and the open MitraClip in the left ventricle may further impede leaflet visualization because of shadowing of the posterior leaflet by the annuloplasty ring. In cases of ring dehiscence, the ring may conflict with the delivery system, create

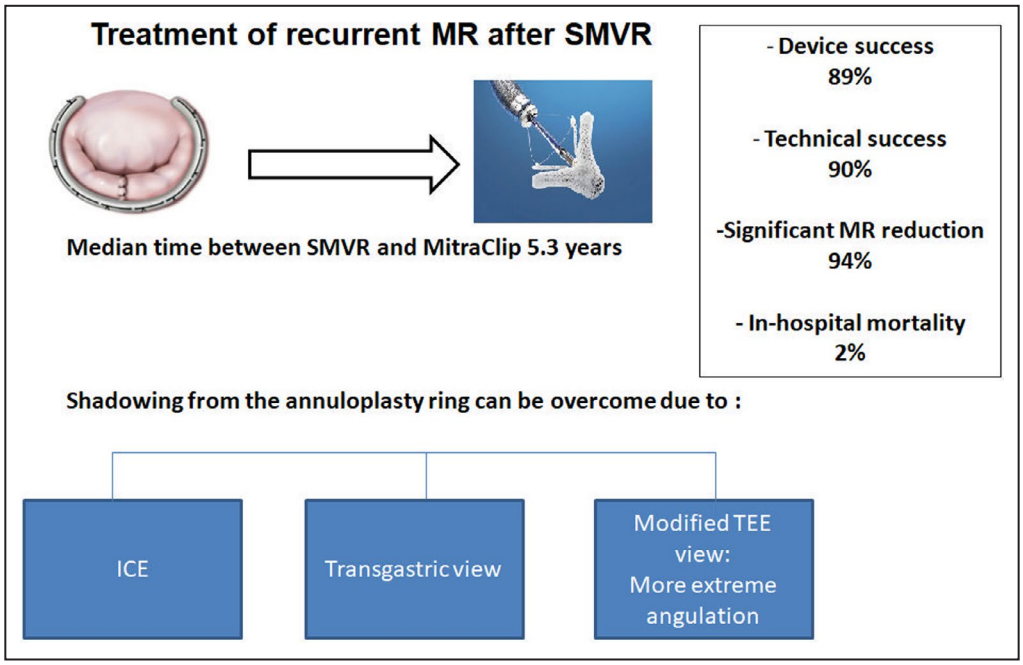

Figure 2. Overview of the main outcomes of this study.
ICE indicates intracardiac echocardiography; MR, mitral regurgitation; SMVR, surgical mitral valve repair; and TEE, transesophagal echocardiography.

shadowing, and sometimes impede passing of the clip into the left ventricle. A transgastric short-axis view may then offer improved visualization of both leaflets to assist proper and controlled leaflet grasping (Figure 4). In some cases, the surgical ring could induce an inflow gradient, which may further increase after leaflet grasping leading

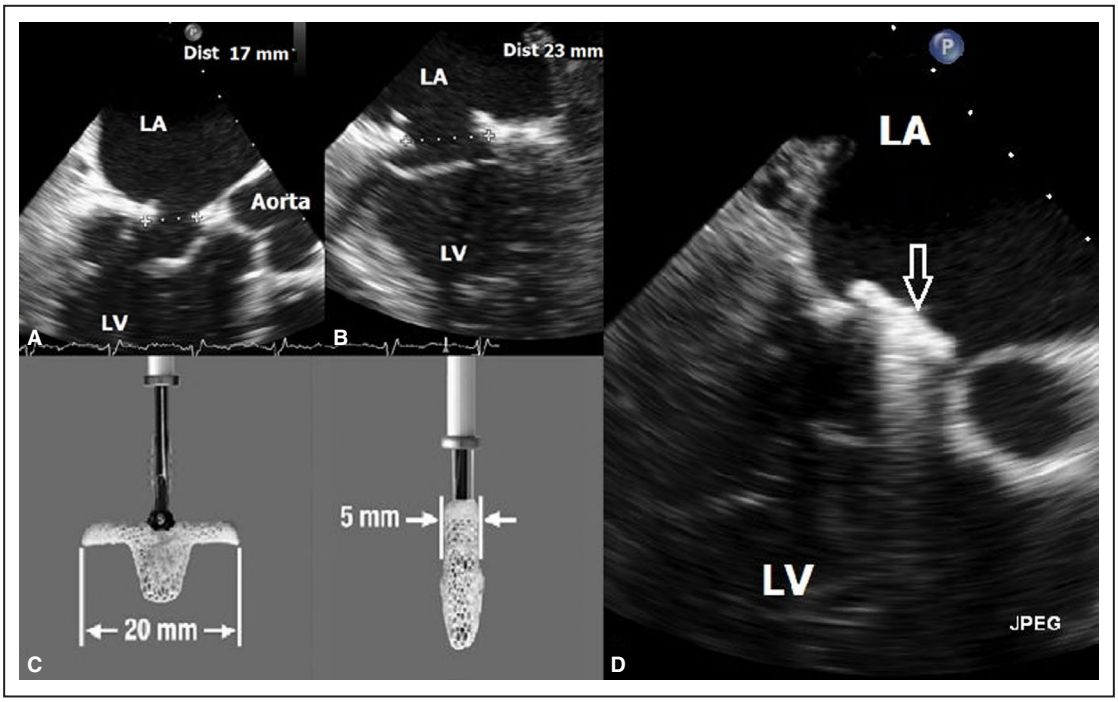

Figure 3. Case example in which the mitral annuloplasy ring precluded crossing of the MitraClip in an open configuration.
A and **B**, The dimensions of the mitral annuloplasty ring measured with transesophageal echocardiography. (**A**) The anterior-posterior diameter and (**B**) the medial-lateral diameter. **C**, The length of the MitraClip with open and closed arms. **D**, MitraClip in open configuration was not able to cross the surgical mitral ring. Arrow indicates MitraClip; LA, left atrium; and LV, left ventricle.

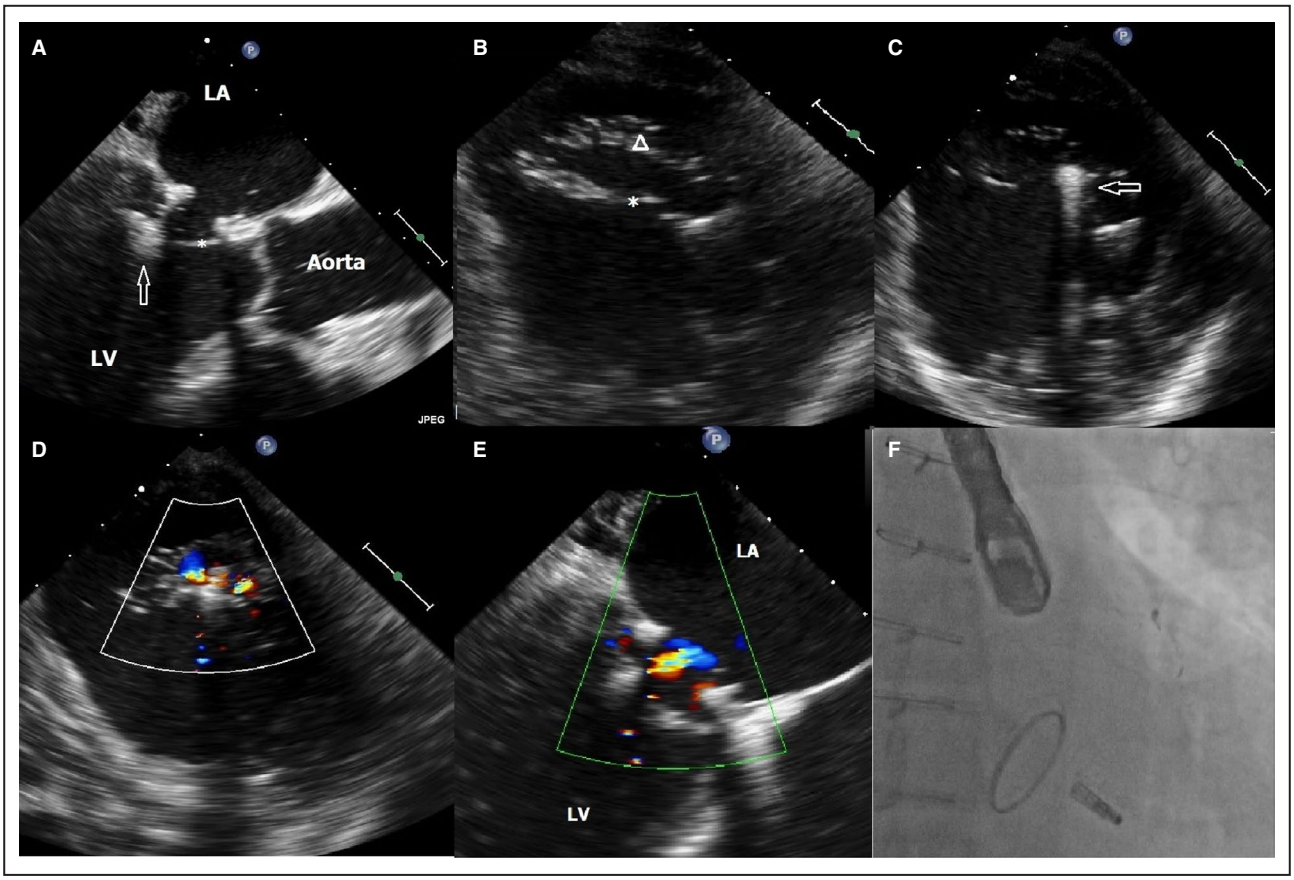

Figure 4. Additional value of the transgastric view during MitraClip grasping.
A, Poor visualization of the posterior leaflet in the long-axis view. **B**, Excellent visualization of both mitral valve leaflets in the transgastric view. **C**, The transgastric view was used during the grasping process and (**D** and **E**) resulted in significant mitral regurgitation reduction (**F**) after the implantation of a MitraClip. Arrow indicates MitraClip; LA, left atrium; and LV, left ventricle. *Anterior mitral valve leaflet; Δ posterior mitral valve leaflet.

to mitral stenosis. Consequently, operators may decide not to release the clip. Postprocedural mitral stenosis (ie, transvalvular mitral gradient measured invasively >5 mm Hg or echocardiographically >4.4 mm Hg) after MitraClip has been shown to have a negative impact on long-term outcome.[24] Invasive transmitral pressure

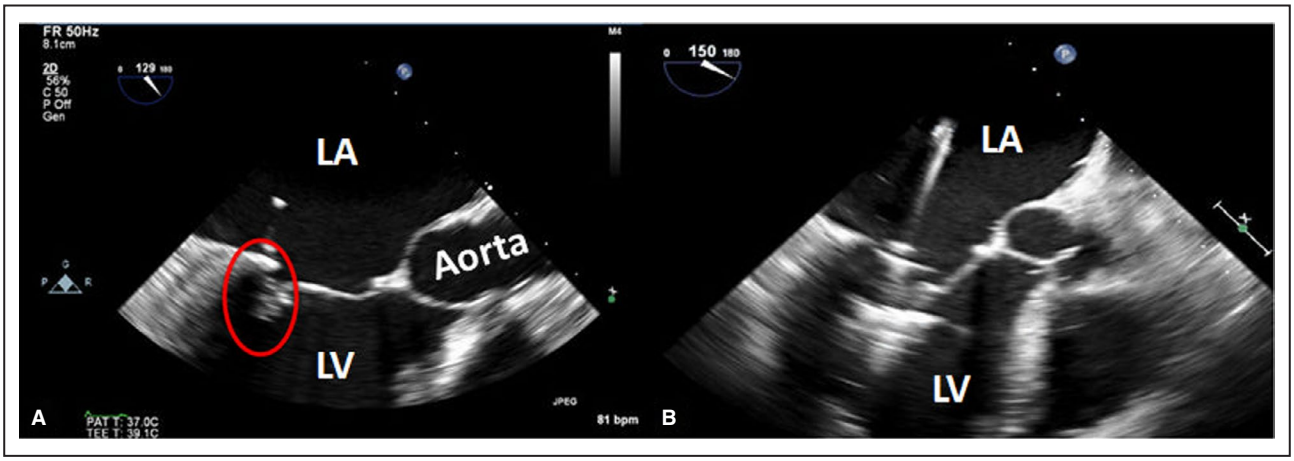

Figure 5. Case example in which more extreme transesophageal echocardiography angulation optimized visualization of the posterior leaflet.
A, Poor visualization of the posterior leaflet with the standard transesophageal echocardiography view (indicated by the red circle). **B**, More extreme angulation offered better visualization of the posterior leaflet. LA indicates left atrium; and LV, left ventricle.

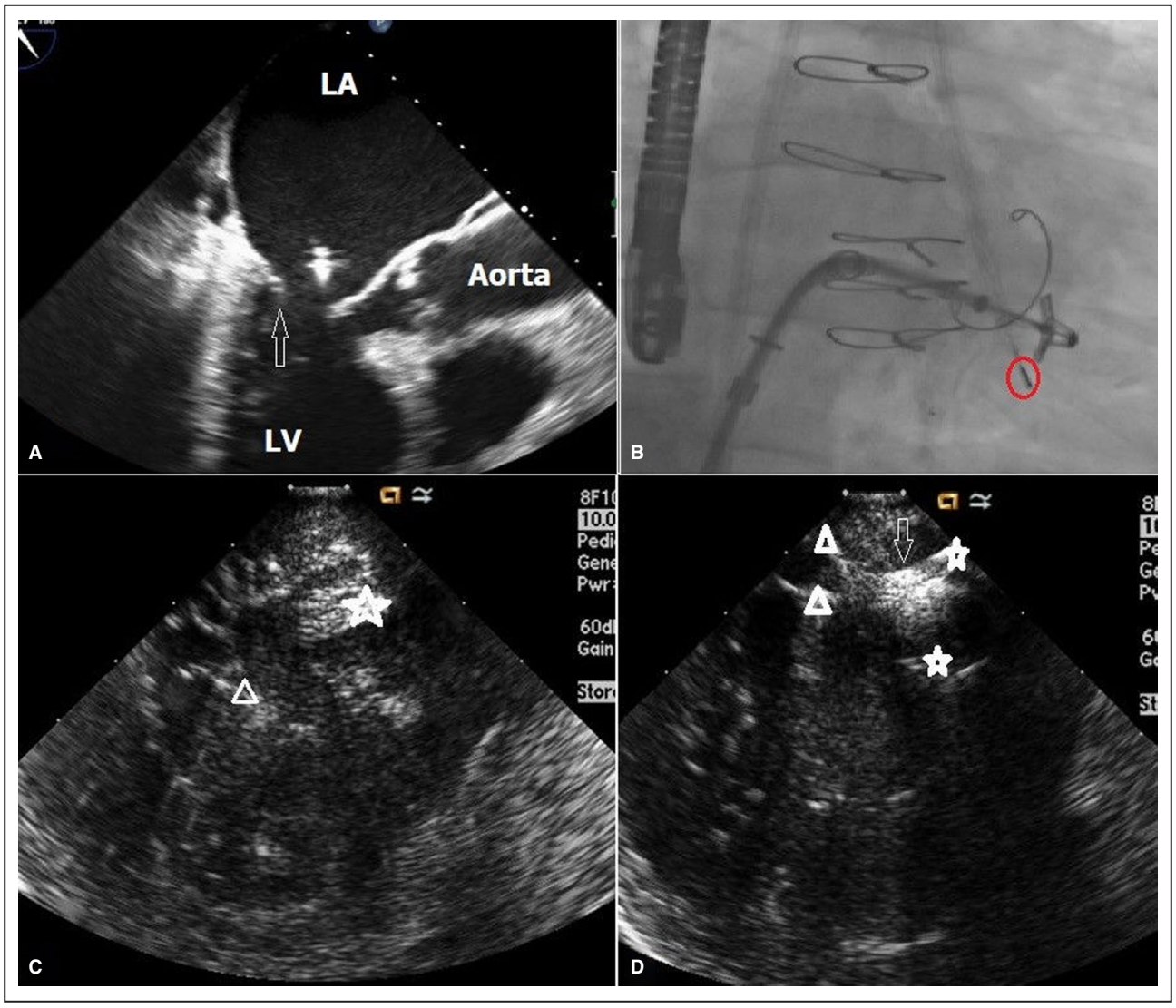

Figure 6. Additional value of intracardiac echocardiography in the visualization of both mitral valve leaflets.
A, Transesophageal echocardiographic image showing shadowing of the posterior leaflet (indicated by the arrow). **B**, Intracardiac echocardiographic catheter in the left ventricle (LV; indicated by the red circle). **C** and **D**, Short-axis LV visualization including both mitral valve leaflets (*anterior mitral valve leaflet; Δ posterior mitral valve leaflet; arrow MitraClip). LA indicates left atrium.

monitoring may further guide MitraClip implantation in this setting.[25]

Poor visualization of the posterior leaflet caused by shadowing from the annuloplasty ring can often be addressed by manipulation of the transesophageal echocardiography probe to move the imaging element relatively more left lateral within the esophagus (Figure 5). This maneuver will often reposition the image of the posterior mitral leaflet so that it does not fall within the surgical ring shadow. In general, atypical multiplanar angles or adjustment wheel manipulation may be necessary to view the complete leaflet grasping zone. Alternatively, the MitraClip may be deployed without complete visualization of the posterior leaflet but with the knowledge that the leaflet is often vertically oriented and under chordal restriction, which limits the concern for leaflet curling within the device closure zone.

In selected cases in which confirmation of the insertion of the posterior leaflet into the MitraClip could not be achieved by standard or modified imaging planes of the transesophageal probe, some investigators have used adjunctive intracardiac echocardiography (Figure 6 and Video S1). Both venous and arterial approaches have been used to position the intracardiac echocardiography catheter in order to obtain a clear view of the anterior and posterior leaflet and visualize grasping and clipping maneuvers. Conceivably, further intracardiac echocardiography iterations (eg, 4-dimensional technology) may enhance mitral valve imaging in the near future.

In our study, patients were treated with the MitraClip NT device (Abbott Vascular). Additional device sizes

are emerging and may generate a more individualized/patient tailored approach.

Another minimally invasive alternative for redo surgery in the setting of prior surgical mitral repair is transcatheter mitral valve replacement. Device success and 30-day all-cause mortality with transcatheter mitral valve replacement in prior surgical ring are 69.5% and 9.9%, respectively.[11]

An important and potentially fatal complication is LV obstruction. Small LV cavity, septal hypertrophy, length of the anterior mitral valve leaflet, and aorto-mitral angle <120° are important risk factors for LV outflow tract obstruction.[11,26–28] Therefore, these anatomic characteristics favor MitraClip treatment.

Limitations

The retrospective nature of our research is susceptible to selection bias. There was no echo-core laboratory or clinical event committee for completely independent data analysis. The modest patient population, limited follow-up, and the lack of a standardized echocardiography protocol should be acknowledged. Furthermore, the overall recurrence rate of MR after failed SMVR was missing in this study. Still, this is the largest cohort to date confirming the safety and efficacy of MitraClip treatment in patients with prior SMVR. Larger trials with longer follow-up data are needed to assess long-term efficacy.

CONCLUSIONS

MitraClip is a safe and minimally invasive treatment option for patients with recurrent MR after failed SMVR. Additional/modified imaging may help overcome technical challenges during leaflet grasping.

ARTICLE INFORMATION

Received September 2, 2020; accepted February 1, 2021.

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Acknowledgments

We acknowledge A. Englmaier from Medizinische Klinik I der Ludwig-Maximilians Universität München for data collection.

Sources of Funding

None.

Disclosures

Lim reports that his institution receives research grants from Abbott Vascular and Edwards Lifesciences, and he reports personal consulting income from Abbott Vascular and Edwards Lifesciences. Hausleiter reports that his institution receives research grants from Abbott Vascular and Edwards Lifesciences, and he received speaker honoraria from Abbott Vascular and Edwards Lifesciences and serves as a consultant for both companies. Taramasso is a consultant for Abbott, Boston Scientific, 4tech, and CoreMedic; reports personal fees from Edwards and CardioValve; and is on the advisory board for Abbott. Estevez-Loureiro is consultant for Abbott Vascular. Delgado received speaker fees from Abbott Vasculer, Edwards Lifesciences, GE Healthcare, and Medtronic. Bax received speaker fees from Abbott Vascular. The Department of Cardiology of the Leiden University Medical Center received grants from Abbott Vascular, Bayer, Biotronik, Bioventrix, Boston Scientific, Edwards Lifesciences, GE Healthcare, and Medtronic. Maisano reports grant and/or research support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, and Terumo; consulting fees/honoraria from Abbott, Medtronic, Edwards Lifesciences, Swissvortex, Perifect, Xeltis, Transseptal solutions, Cardiovalve, and Magenta; royalty income/IP rights from Edwards Lifesciences; and is a shareholder of Cardiovalve, Cardiogard, Magenta, SwissVortex, Transseptalsolutions, Occlufit, 4Tech, and Perifect. Sorajja reports personal fees from Abbott Structural; personal fees from Medtronic, Boston Scientific, Edwards, Admedus, Gore, and Teleflex, outside of the submitted work. Piazza is proctor for HighLife and is a steering committee member of Medtronic's Apollo Trial. Van Mieghem reports research grant support and advisory fees from Abbott, Boston Scientific, and Medtronic. Little reports personal fees from Abbott Structural Heart and Medtronic Structural Heart, outside of the submitted work. Latib reports personal fees from Medtronic, Abbott Vascular, and Edwards Lifesciences, outside of the submitted work. Castriota reports personal fees from Abbott Vascular, outside of the submitted work. Braun reports speaker honoraria from Abbott Vascular. The remaining authors have no disclosures to report.

Supplementary Material

Video S1

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