4-26-2021

Prospective Evaluation of TMVR for Failed Surgical Annuloplasty Rings: MITRAL Trial Valve-in-Ring Arm 1-Year Outcomes

Mayra Guerrero

Dee Dee Wang
Henry Ford Health, dwang2@hfhs.org

Amit Pursnani

Michael Salinger

Hyde M. Russell

See next page for additional authors

Recommended Citation

Guerrero M, Wang DD, Pursnani A, Salinger M, Russell HM, Eleid M, Chakravarty T, Eng MH, Kodali SK, Meduri CU, Pershad A, Satler L, Waksman R, Palacios I, Smalling R, Reisman M, Gegenhuber M, Kaptzan T, Lewis B, Tommaso C, Krause P, Thaden J, Oh J, Douglas PS, Hahn RT, Kar S, Makkar R, Leon MB, Feldman T, Rihal C, and O'Neill WW. Prospective Evaluation of TMVR for Failed Surgical Annuloplasty Rings: MITRAL Trial Valve-in-Ring Arm 1-Year Outcomes. JACC Cardiovasc Interv 2021; 14(8):846-858.

Authors

Mayra Guerrero, Dee Dee Wang, Amit Pursnani, Michael Salinger, Hyde M. Russell, Mackram Eleid, Tarun Chakravarty, Marvin H. Eng, Susheel K. Kodali, Christopher U. Meduri, Ashish Pershad, Lowell Satler, Ron Waksman, Igor Palacios, Richard Smalling, Mark Reisman, Mary Gegenhuber, Tatiana Kaptzan, Brad Lewis, Carl Tommaso, Philip Krause, Jeremy Thaden, Jae Oh, Pamela S. Douglas, Rebecca T. Hahn, Saibal Kar, Raj Makkar, Martin B. Leon, Ted Feldman, Charanjit Rihal, and William W. O'Neill

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 8, 2021

PUBLISHED BY ELSEVIER

Prospective Evaluation of TMVR for Failed Surgical Annuloplasty Rings

MITRAL Trial Valve-in-Ring Arm 1-Year Outcomes

Mayra Guerrero, MD,[a] Dee Dee Wang, MD,[b] Amit Pursnani, MD,[c] Michael Salinger, MD,[d] Hyde M. Russell, MD,[e] Mackram Eleid, MD,[a] Tarun Chakravarty, MD,[f] Marvin H. Ng, MD,[b] Susheel K. Kodali, MD,[g] Christopher U. Meduri, MD,[h] Ashish Pershad, MD,[i,*] Lowell Satler, MD,[j] Ron Waksman, MD,[j] Igor Palacios, MD,[k] Richard Smalling, MD,[l] Mark Reisman, MD,[m,†] Mary Gegenhuber, RN,[n] Tatiana Kaptzan, PhD,[o] Brad Lewis, MS,[p] Carl Tommaso, MD,[c] Philip Krause, MD,[c] Jeremy Thaden, MD,[a] Jae Oh, MD,[a] Pamela S. Douglas, MD,[q] Rebecca T. Hahn, MD,[g] Saibal Kar, MD,[r] Raj Makkar, MD,[f] Martin B. Leon, MD,[g] Ted Feldman, MD,[s] Charanjit Rihal, MD,[a] William W. O'Neill, MD[b]

ABSTRACT

OBJECTIVES The authors report 1-year outcomes of high-risk patients with failed surgical annuloplasty rings undergoing transseptal mitral valve-in-ring (MViR) with the SAPIEN 3 aortic transcatheter heart valve (THV).

BACKGROUND The MITRAL (Mitral Implantation of Transcatheter Valves) trial is the first prospective study evaluating transseptal MViR with the SAPIEN 3 aortic THV in high-risk patients with failed surgical annuloplasty rings.

METHODS Prospective enrollment of high-risk patients with symptomatic moderate to severe or severe mitral regurgitation (MR) or severe mitral stenosis and failed annuloplasty rings at 13 U.S. sites. The primary safety endpoint was technical success. The primary THV performance endpoint was absence of MR grade ≥2+ or mean mitral valve gradient ≥10 mm Hg (30 days and 1 year). Secondary endpoints included procedural success and all-cause mortality (30 days and 1 year).

RESULTS Thirty patients were enrolled between January 2016 and October 2017 (median age 71.5 years [interquartile range: 67.0 to 76.8 years], 36.7% women, median Society of Thoracic Surgeons score 7.6% [interquartile range: 5.1% to 11.8%], 76.7% in New York Heart Association functional class III or IV). Technical success was 66.7% (driven primarily by need for a second valve in 6 patients). There was no intraprocedural mortality or conversion to surgery. The primary performance endpoint was achieved in 85.7% of survivors at 30 days (24 of 28) and 89.5% of patients alive at 1 year with echocardiographic data available (17 of 19). All-cause mortality at 30 days was 6.7% and at 1 year was 23.3%. Among survivors at 1-year follow-up, 84.2% were in New York Heart Association functional class I or II, the median mean mitral valve gradient was 6.0 mm Hg (interquartile range: 4.7 to 7.3 mm Hg), and all had ≤1+ MR.

CONCLUSIONS Transseptal MViR was associated with a 30-day mortality rate lower than predicted by the Society of Thoracic Surgeons score. At 1 year, transseptal MViR was associated with symptom improvement and stable THV performance. (J Am Coll Cardiol Intv 2021;14:846–58) © 2021 by the American College of Cardiology Foundation.

From the [a]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA; [b]Center for Structural Heart Disease, Henry Ford Hospital, Detroit, Michigan, USA; [c]Division of Cardiology, NorthShore University HealthSystem, Evanston, Illinois, USA; [d]Division of Cardiology, Froedtert Medical College of Wisconsin, Milwaukee, Wisconsin, USA; [e]Division of Cardiovascular Surgery, NorthShore University HealthSystem, Evanston, Illinois, USA; [f]Department of Cardiology, Cedars-Sinai Heart Institute, Los Angeles, California, USA; [g]Division of Cardiology Columbia University Medical Center, New York, New York, USA; [h]Division of Cardiology, Piedmont Hospital, Atlanta, Georgia, USA; [i]Division of Cardiology, Banner University Medical Center, Phoenix, Arizona, USA; [j]Division of Cardiology, Medstar Washington Hospital Center, Washington, DC, USA; [k]Division of Cardiology, Massachusetts General Hospital, Boston, Massachusetts, USA; [l]Division of Cardiology, Memorial Hermann Heart and Vascular Center, Texas Medical Center, Houston, Texas, USA; [m]Division of Cardiology, University of Washington Medical Center, Seattle, Washington, USA; [n]Novartis Gene Therapies, Bannockburn, Illinois, USA; [o]Cardiovascular Research Unit, Mayo Clinic, Rochester, Minnesota, USA; [p]Division of Biostatistics and Informatics, Mayo Clinic, Rochester, Minnesota, USA; [q]Duke Clinical Research Institute, Duke University, Durham, North Carolina, USA; [r]Division of Cardiology, Los Robles Regional Medical Center, Thousand Oaks, California, USA; and [s]Edwards Lifesciences, Irvine, California, USA. *Dr. Pershad is currently affiliated with the Division of

ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2021.01.051

Despite increases in surgical volumes and experience, contemporary 30-day mortality related to repeat mitral surgery remains higher (11.1%) than that associated with a first mitral valve (MV) operation (6.5%; $p < 0.0001$) (1).

Transcatheter MV replacement (TMVR) using balloon-expandable aortic transcatheter heart valves (THVs) has emerged as an alternative to surgery for patients with severe MV disease due to failed surgical repairs with annuloplasty rings, among those who are not good candidates for conventional MV surgery. Retrospective registries collecting early experience of mitral valve-in-ring (MViR) procedures using the SAPIEN family of aortic THVs (Edwards Lifesciences, Irvine, California) in patients at high surgical risk have shown that MViR is feasible with reasonable outcomes. The 30-day mortality rate in the early experience of the VIVID (Valve in Valve International Data) registry was 11.4% and in the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) Registry was 11.5% (2,3). These 2 registries collected early experience, including first- and second-generation devices and a large proportion of transapical access. Whether newer generation devices and/or the use of transseptal access will result in improved outcomes is not known. A prospective clinical trial had not been performed prior to our study. The aim of the MViR arm of the MITRAL (Mitral Implantation of Transcatheter Valves) trial (IDE G140136; NCT02370511) is to prospectively evaluate the safety and feasibility of transseptal MViR using the third-generation SAPIEN 3 valve in patients who are not candidates for conventional redo mitral surgery. We present herein the 1-year outcomes of MViR in this trial.

SEE PAGE 873

METHODS

The MITRAL early feasibility study is a physician-initiated, prospective, multicenter, clinical trial designed to evaluate the safety and feasibility of TMVR using the SAPIEN XT and SAPIEN 3 valves. The study has 3 treatment arms: native MV disease with severe mitral annular calcification (MAC) treated with valve-in-MAC procedures, failing surgical repairs with annuloplasty rings treated with MViR, and mitral valve-in-valve (MViV) in failed surgical bioprostheses. A total of 91 patients at high surgical risk were enrolled (valve-in-MAC, n = 31; MViR, n = 30; MViV, n = 30) and treated between March 2015 and December 2017 at 13 sites in the United States. We present herein the results of the MViR arm. Patients were considered eligible for the study if they had symptoms of New York Heart Association functional class II or greater due to severe mitral stenosis, defined as MV area 1.5 cm^2 or less by transthoracic echocardiography or at least moderate to severe mitral regurgitation (MR). A list of inclusion and exclusion criteria is provided in Supplemental Appendix 1.

Candidates were presented in a live case-review conference call to a subject eligibility committee to determine eligibility. Baseline echocardiograms and computed tomographic (CT) studies were analyzed by independent core laboratories. Clinical events were adjudicated by an independent clinical events committee, and safety was monitored by a data and safety monitoring board (Supplemental Appendix 2). This study was conducted following ethical principles according to the Declaration of Helsinki as well as U.S. Food and Drug Administration guidelines (Code of Federal Regulations Title 21, Part 812) and Good Clinical Practices recommended by the International Organization for Standardization (ISO 14155:2011). The study was approved by the Mayo Clinic Institutional Review Board and the respective Institutional Review Boards of the participating institutions. All patients provided written informed consent.

PROCEDURES. Transthoracic and transesophageal echocardiograms were obtained according to published guidelines and were analyzed at an independent core laboratory according to the American Society of Echocardiography standard for echocardiography core laboratories (4,5). The cardiac CT image acquisition protocol was similar to CT protocols for transcatheter aortic valve replacement (6), with adjustments for MV analysis (7), summarized in Supplemental Appendix 3 and illustrated in **Figure 1**. Although the MViV software application was used in the evaluation (8), THV size was selected according to

ABBREVIATIONS AND ACRONYMS

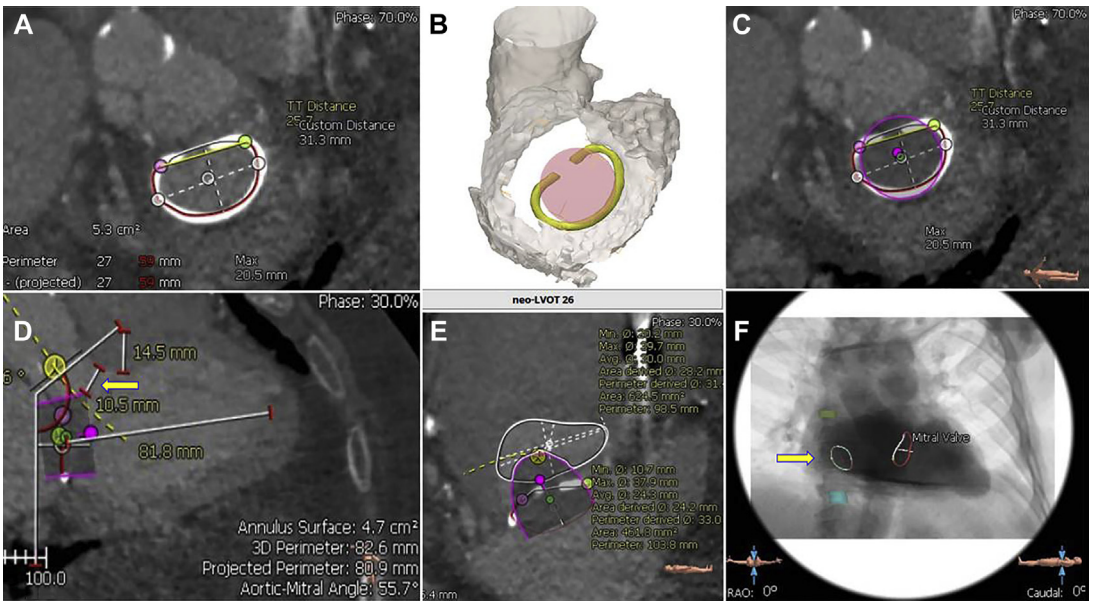
CT = computed tomographic
LVOT = left ventricular outflow tract
MAC = mitral annular calcification
MR = mitral regurgitation
MV = mitral valve
MVG = mitral valve gradient
MViR = mitral valve-in-ring
MViV = mitral valve-in-valve
THV = transcatheter heart valve
TMVR = transcatheter mitral valve replacement

Cardiology, Chandler Regional and Mercy Gilbert Medical Center, Gilbert, Arizona, USA. †Dr. Reisman is currently affiliated with the Weill Medical Center, New York, New York, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

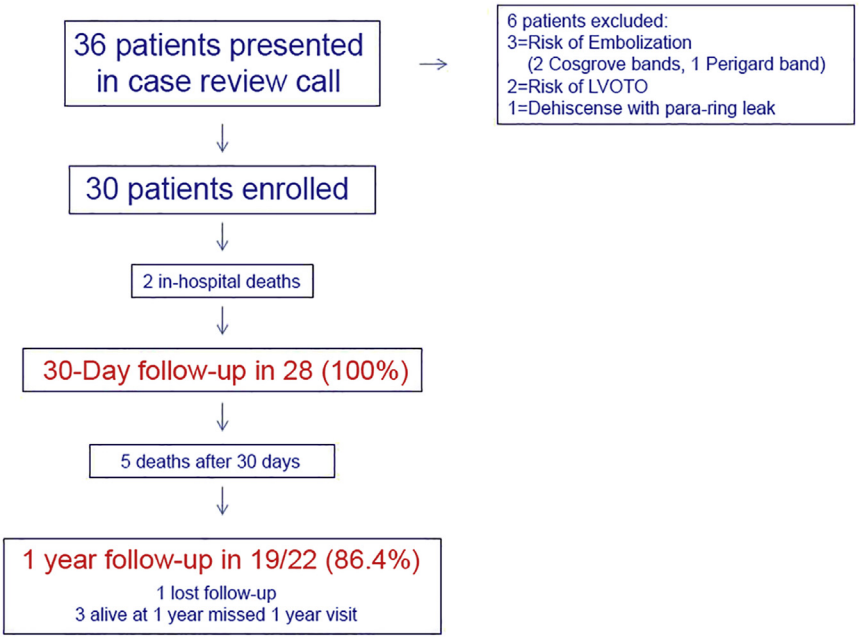
Manuscript received December 4, 2020; revised manuscript received January 15, 2021, accepted January 19, 2021.

FIGURE 1 Cardiac Computed Tomographic Analysis



Measurements of mitral annulus made using 3mensio Structural Heart Workflow version 8.1 (Pie Medical Imaging, Maastricht, the Netherlands). **(A)** The mitral valve "neo-annulus" area of surgical ring measurement is shown from the surgeon's short-axis view during diastole (D-shape method). **(B,C)** A virtual transcatheter heart valve (THV) is placed in the mitral surgical ring **(pink)**, with size selected according to neo-annulus/surgical ring area. **(D)** The virtual valve placed in the mitral annulus is visualized in the left ventricular outflow tract (LVOT) long-axis view. The LVOT space is measured at the site where the THV stent frame is in closest proximity of the septum **(arrow)**. **(E)** Neo-LVOT area measurement shown in short-axis view during systole. After placing the virtual valve **(pink)**, the remaining LVOT area is measured **(white)**. **(F)** Fluoroscopic simulation of transseptal access **(arrow)** for procedural planning purposes.

FIGURE 2 Patient Flowchart



LVOTO = left ventricular outflow tract obstruction.

TABLE 1 Baseline Patient Characteristics (n = 30)

Age (yrs)	71.5 (67.0–76.8)
Female	11/30 (36.7)
Diabetes	9/30 (30)
Atrial fibrillation	21/30 (70)
Chronic kidney disease	10/30 (33.3)
Chronic obstructive pulmonary disease	6 /30 (20)
Home oxygen therapy	4/30 (13.3)
Receiving long-term anticoagulation	15/30 (50)
Hospitalization for heart failure during prior 12 months	9/30 (30)
Prior stroke	4/30 (13.3)
Prior CABG	19/30 (63.3)
Prior AVR	4/30 (13.3)
TAVR	1/4 (25)
SAVR	3/4 (75)
Type of surgical ring	
Edwards Physio	9/30 (30)
Edwards Classic	4/30 (13.3)
S. Jude Seguin	3/30 (10)
Medtronic CG Future Ring	3/30 (10)
Medtronic CG Future Band	2/30 (6.7)
Edwards Physio 2	2/30 (6.7)
Edwards ET Logix	1/30 (3.3)
St. Jude Tailor Band	1/30 (3.3)
Medtronic Simulus SemiRigid	1/30 (3.3)
Duran AnCore	1/30 (3.3)
Sorin Memo 3D	1/30 (3.3)
Sorin Annuloflex	1/30 (3.3)
Cosgrove band	1/30 (3.3)
STS score for MVR	7.6 (5.1–11.8)
NYHA functional class	
I	0/30 (0)
II	7/30 (23.3)
III	20/30 (66.7)
IV	3/30 (10)

Values are median (interquartile range) or n/N (%).

AVR = aortic valve replacement; CABG = coronary artery bypass grafting; MVR = mitral valve replacement; NYHA = New York Heart Association; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

TABLE 2 Baseline Echocardiographic Characteristics (n = 30)

Ejection fraction (%)	46.5 (33.4–55.6)
Stroke volume (ml)	64.6 (52.1–81.8)
Cardiac output (l/min)	5.2 (3.7–5.8)
Mean MVG (mm Hg)	6.2 (4.6–8.2)
MVA (cm^2)	2.8 (2.3–3.2)
Pulmonary artery systolic pressure (mm Hg)*	46.5 (40.5–59.8)
Peak LVOT gradient (mm Hg)	3.3 (2.5–4.5)
Mean LVOT gradient (mm Hg)	1.6 (1.3–2.4)
Pathology (mode of ring failure)	
Stenosis	10/30 (33.3)
Regurgitation	17/30 (56.7)
Both stenosis and regurgitation	3/30 (10)
Severity of mitral regurgitation	
None or trace	5/30 (16.7)
1 (+)	5/30 (16.7)
2 (+)	12/30 (40.0)
3 (+)	7/30 (23.3)
4 (+)	1/30 (3.4)

Values are median (interquartile range) or n/N (%). *Five missing.

LVOT = left ventricular outflow tract; MVA = mitral valve area; MVG = mitral valve gradient.

the mitral neo-annulus area as determined by cardiac CT analysis using a sizing chart, as done for transcatheter aortic valve replacement (7,9). All patients were treated with transseptal access. The preferred location for transseptal puncture was inferior and posterior. Balloon septostomy for transseptal delivery of the THV was performed using a 10- or 12-mm balloon for the 23- and 26-mm SAPIEN 3 valves and a 12- or 14-mm balloon for the 29-mm valve. The technique for transseptal MViR is similar to the previously published transseptal MViV technique (7).

OUTCOMES. The primary safety endpoint was technical success at exit from the cardiac catheterization laboratory, defined as successful delivery and retrieval of the transcatheter delivery system, deployment of a single valve in the correct position in the mitral annulus, adequate performance of the THV with residual MR <2+ and mean MV gradient (MVG) <10 mm Hg, no need for surgery or additional reintervention, and patient's departure from the procedure room alive. The primary THV performance endpoint was absence of MR grade ≥2+ or mean MVG ≥10 mm Hg at 30 days and 1 year. Secondary safety endpoints included procedural success and all-cause mortality at 30 days and 1 year. Definitions and a complete list of secondary endpoints are provided in Supplemental Appendix 4.

STATISTICAL ANALYSIS. Continuous variables are summarized as median (interquartile range). Categorical variables are presented as frequencies and percentages. Comparisons between time points were made using a Wilcoxon test. Comparisons of mean MVG between THV sizes were made using Kruskal-Wallis 1-way analysis of variance on ranks. A Kaplan-Meier curve was generated for all-cause mortality and the composite endpoint of all-cause mortality and hospitalization for heart failure. For the purposes of this paper, all p values were 2-sided, and values <0.05 were considered to indicate statistical significance. All analyses were conducted using R version 3.6.2 (R Foundation for Statistical Computing, Vienna Austria).

RESULTS

Between January 2016 and October 2017, 36 subjects were screened and presented at a case-review

TABLE 3 Intraprocedural Results (n = 30)

Device	
SAPIEN 3	30/30 (100)
Device size	
23 mm	6/30 (20)
26 mm	16/30 (53.3)
29 mm	8/30 (26.7)
Access	
Transeptal	30/30 (100)
Pre-dilation or balloon sizing*	11/30 (36.7)
Additional contrast during initial deployment	
No	13/30 (43.3)
Yes	17/30 (56.7)
Amount (ml)	4 (0-5)
Post-dilatation	12/30 (40)
Septostomy closed	4/30 (13.3)
Results	
In-hospital mortality	2/30 (6.7)
Cardiovascular	2/30 (6.7)
Noncardiovascular	0/30 (0)
Technical success at exit from catheterization laboratory	20/30 (66.7)
LVOT obstruction with hemodynamic compromise	0/30 (0)
Need for a second valve	6/30 (20)
≥2 (+) MR on procedural TEE	3/30 (10)
Paravalvular leak closure during index procedure	1/30 (3.3)
Vascular complications	0/30 (0)
Conversion to open heart surgery	0/30 (0)
Valve embolization	0/30 (0)
Left ventricular perforation	0/30 (0)
Pericardial effusion requiring pericardiocentesis	0/30 (0)
New pacemaker requirement	0/30 (0)
Myocardial infarction requiring intervention	0/30 (0)
Echocardiographic characteristics post-TMVR	
Mean MVG (mmHg)	2.9 (2.3-3.9)
MVA (cm^2)	2.9 (2.3-3.6)
Peak LVOT gradient (mm Hg)†	3.6 (2.4-6.6)
Mean LVOT gradient (mm Hg)†	1.8 (1.2-3.5)
Residual MR at end of procedure	
Trace or none	15/30 (50.0)
1 (+)	12/30 (40.0)
2 (+)	3/30(10.0)
≥3 (+)	0/30 (0)
Amount of paravalvular MR at end of procedure‡	
Trace or none	19/30 (63.3)
1 (+)	8/30 (26.7)
2 (+)	3/30 (10.0)
≥3 (+)	0/30 (0)

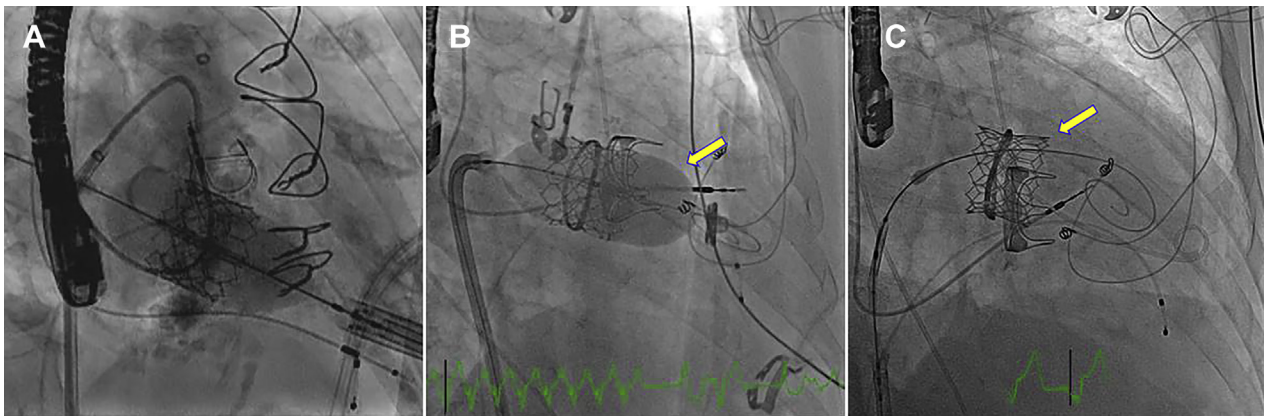
Values are n/N (%) or median (interquartile range). *This represents early experience and occurred at the discretion of the operators if confirmation of sizing was desired. †Fourteen missing. ‡The location of paravalvular leak was at commissures between the transcatheter heart valve and the prosthetic ring (not between the prosthetic ring and the native mitral annulus).

MR = mitral regurgitation; TEE = transesophageal echocardiogram; TMVR = transcatheter mitral valve replacement; other abbreviations as in Tables 1 and 2.

conference call for subject eligibility determination. Six patients (16.7%) were excluded because of suspected high risk for embolization associated with incomplete rings (Cosgrove band, n = 2; PeriGuard band, n = 1), risk for left ventricular outflow tract (LVOT) obstruction (n = 2), and prosthetic ring dehiscence with pararing leak (n = 1). Thirty patients were enrolled (patient flow is illustrated in Figure 2). Baseline clinical characteristics are presented in Table 1. The median age was 71.5 years (interquartile range: 67.0 to 76.8 years), and 36.7% were women. Multiple comorbidities were present, including atrial fibrillation in 70%. The median Society of Thoracic Surgeons Predicted Risk of Mortality score for MV replacement was 7.6% (interquartile range: 5.1% to 11.8%), and 76.7% were in New York Heart Association functional class III or IV. Baseline echocardiographic characteristics are listed in Table 2. Median left ventricular ejection fraction was 46.5% (IQR: 33.4% to 55.6%). MR was the predominant pathology, present in 56.7%.

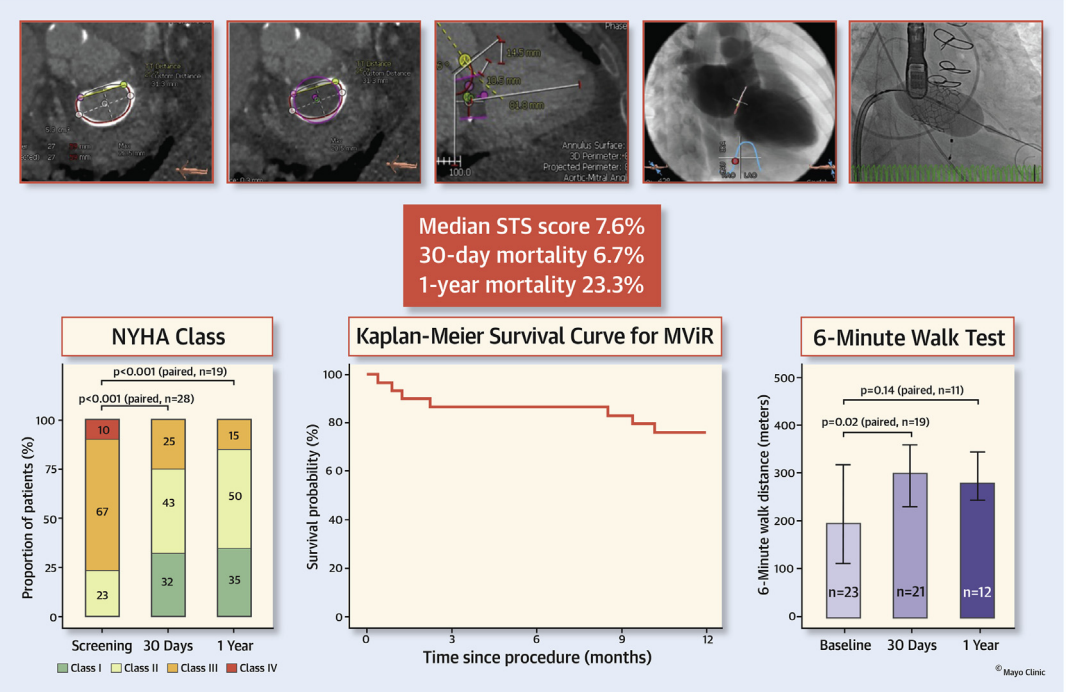
PRIMARY SAFETY ENDPOINT AND SHORT-TERM RESULTS. All patients were treated with transseptal access and with the SAPIEN 3 THV. Procedural results are presented in Table 3. The size of THV chosen according to cardiac CT analysis coincided with the size recommended by the MViV app in 80% of cases. A different size than the one recommended by the MViV app was chosen in 20% (smaller, n = 2; larger, n = 4). The decision to choose a different THV size was based on neo-annulus area by cardiac CT analysis. The THV was prepared with additional contrast volume in the delivery balloon catheter in a majority of cases (56.7%) to flare the THV in the left ventricle to decrease the risk for valve embolization into the left atrium (Figure 3). The primary safety endpoint of technical success at exit from the procedure room was achieved in 66.7% of patients. Reasons for not meeting technical success criteria included need for a second valve (n = 6), mean MVG >10 mm Hg (n = 1), and MR 2+ in 3 patients, of whom 1 was treated with paravalvular leak closure during the index procedure. The paravalvular closure technique has been previously published (10). The reason for the need for a second valve was a too atrial position of the THV resulting in paravalvular leak due to lack of an inner skirt at the annulus level (the inner skirt was mostly on the atrial side above the annulus instead of at the annulus) in 6 patients and invagination of native leaflets leading to MR in 1 patient. These events occurred early in the experience. The landing zone was modified in subsequent cases, aiming for a more ventricular final position of the THV (80% in the ventricle and 20% atrial), which can be achieved by placing the center marker of the THV 1 to 2 mm ventricular to the prosthetic ring during valve deployment. After this modification, the need for a second valve decreased. Rapid pacing and breath-hold were recommended during deployment to increase the probability of proper valve position. The invagination

FIGURE 3 **Additional Contrast Volume in Balloon Delivery System During Valve Deployment**



(A) Transapical valve-in-mitral annular calcification procedure using a 26-mm SAPIEN XT valve prepared with a nominal amount of contrast in the balloon delivery system resulting in a symmetrical cylinder balloon shape. **(B)** Transseptal mitral valve-in-ring procedure using a 29-mm SAPIEN 3 valve prepared with 4 ml additional contrast volume in the balloon delivery system. The additional volume results in flaring of the ventricular edge of the stent frame **(arrow)**. **(C)** After valve deployment, the ventricular edge of the SAPIEN 3 stent frame diameter is larger **(arrow)** than the atrial edge of the stent.

CENTRAL ILLUSTRATION **30-Day and 1-Year Outcomes of Valve-in-Ring in the Mitral Implantation of Transcatheter Valves Trial**



Guerrero, M. et al. J Am Coll Cardiol Intv. 2021;14(8):846-58.

Early and late outcomes for functional capacity (New York Heart Association functional class; **left**), which were significantly improved at both time points versus baseline. Walk distance (meters; median and interquartile range) on 6-min walk test **(right)** also improved. Early mortality (depicted as Kaplan-Meier survival; **middle**) was better than expected on the basis of Society of Thoracic Surgeons score.

TABLE 4 30-Day and 1-Year Clinical Outcomes

	30 Days (n = 30)	1 Year (n = 30)
All-cause mortality	2/30 (6.7)	7/30 (23.3)
Cardiovascular	2/30 (6.7)	2/30 (6.7)
Noncardiovascular	0/30 (0)	5/30 (16.7)
Device success	22/30 (73.3)	NA
Procedural success	22/30 (73.3)	NA
Primary performance endpoint in survivors at 30 days and 1 yr	24/28* (85.7)	17/19† (89.5)
Stroke	1/30 (3.3)	1/30 (3.3)
Ischemic	0/30 (0)	0/30 (0)
Hemorrhagic‡	1/30 (3.3)	1/30 (3.3)
Myocardial infarction requiring revascularization	0/30 (0.0)	0/30 (0.0)
Mitral valve reintervention after index procedure§	2/30 (6.7)	3/30 (10)
Septostomy closed‖	5/30 (16.7)	7/30 (23.3)
Acute kidney injury requiring hemodialysis	3/30 (10)	4/30 (13.3)
Blood transfusion	9/30 (30)	12/30 (40)
Vascular complication¶	2/30 (6.7)	2/30 (6.7)
New permanent pacemaker requirement	0/30 (0)	0/30 (0)
New-onset atrial fibrillation#	1/30 (3.3)	1/30 (3.3)
Patients rehospitalized for heart failure	0/30 (0)	5/30 (16.7)
Hospitalization for heart failure events	0/30 (0)	6/30 (20)
Device embolization or migration**	1/30 (3.3)	1/30 (3.3)
Hemolytic anemia††	1/30 (3.3)	3/30 (10)
Valve thrombosis	0/30 (0)	0/30 (0)
Endocarditis	0/30 (0)	0/30 (0)
New York Heart Association functional class		
I	9/28* (32.1)	7/19† (36.8)
II	12/28 (42.9)	9/19 (47.4)
III	7/28 (25)	3/19 (15.8)
IV	0/28 (0)	0/19 (0)

Values are n/N (%). *2 died within 30 days. †7 died, 1 lost to follow-up, and 3 alive at 1 yr missed 1-yr follow-up. ‡Spontaneous bleeding in a previously undiagnosed pre-existing brain tumor during the index hospitalization. §1 PVL closure attempt followed by surgical MVR and 1 transseptal mitral valve-in-valve plus PVL closure within 30 days. 1 PVL closure between 30 days and 1 yr. ‖4 during index procedure, 1 between discharge and 30-day follow up, 2 between 30-day and 1-yr follow-up. ¶Retroperitoneal bleeding during index hospitalization. #After open heart surgery in a patient who underwent conventional surgical MVR because of PVL. **After chest compressions during cardiopulmonary resuscitation for an aspiration event resulting in respiratory arrest. Device migration caused PVL. The patient underwent PVL closure. ††1 prior to discharge treated with PVL closure attempt followed by surgical MVR. One more after 30 days treated conservatively.

MVR = mitral valve repair; NA = not applicable; PVL = paravalvular leak.

of native leaflets occurred in the setting of a long anterior leaflet overriding the ventricular edge of the stent. This was successfully treated with a second THV placed in a more ventricular position than the initial THV. There were no cases of LVOT obstruction, intraprocedural mortality, or conversion to open heart surgery. Atrial septostomy was closed percutaneously in 4 patients during the index procedure (13.3%), at the discretion of the operator because of a large left-to-right shunt in 3 patients and thrombus in a right atrial pacemaker lead in 1 patient.

ADDITIONAL ENDPOINTS. The primary THV performance endpoint of absence of MR grade 2+ or greater or mean MVG ≥10 mm Hg was achieved in 85.7% of the 28 survivors at 30 days (24 of 28) and 89.5% of patients alive at 1 year with echocardiographic data available (17 of 19). The secondary safety endpoint of procedural success was achieved in 22 patients (73.3%). Reasons for not achieving procedural success in 8 subjects included death (n = 2), mean MVG 10 mm Hg (n = 4), hemolysis requiring paravalvular leak closure attempt followed by conventional MV surgical replacement (n = 1), and intracranial hemorrhage without neurological sequelae (n = 1). All-cause mortality at 30 days was 6.7% and at 1 year was 23.3%. The Kaplan-Meier survival curve is presented in Figure 3 and the Central Illustration.

30-DAY OUTCOMES. At 30-day follow-up, 93.3% of the patients were alive (28 of 30) and 75% were in New York Heart Association functional class I or II. The 2 deaths observed within 30 days occurred during the index hospitalization, one due to heart failure decompensation and the other to THV migration after chest compressions during cardiopulmonary resuscitation for an aspiration event resulting in respiratory arrest. This patient had undergone uneventful MViR in a semirigid ring and met the criteria for technical success. The valve migration after chest compressions caused significant MR, treated with a paravalvular leak closure procedure and transseptal MViV. The patient died 2 days later of ventricular fibrillation cardiac arrest. Clinical events at 30 days and 1 year are presented in Table 4 and echocardiographic characteristics in Table 5. Only 1 patient had a stroke (3.3%), which was a spontaneous intracranial hemorrhage during the index hospitalization in a pre-existing, previously undiagnosed brain tumor. The event did not result in clinical sequalae. One patient underwent septostomy closure between discharge and 30-day follow-up, due to heart failure attributed to a left-to-right shunt. Two patients (6.7%) required MV reintervention: 1 paravalvular leak closure attempt followed by surgical MV replacement for hemolytic anemia and 1 transseptal MViV plus paravalvular leak closure for MR related to valve migration. Hemolytic anemia was rare and was present in only 1 patient within 30 days (3.3%). There were no THV thromboses or endocarditis events.

30-DAY OUTCOMES IN PATIENTS WHO NEEDED A SECOND VALVE DURING THE INDEX PROCEDURE. Although the 6 patients who needed a second valve during the index procedure to treat MR resulting from a too atrial position of the THV did not meet criteria for technical success, there were no adverse consequences. All of them were alive at 30 days and met the criteria for device success, procedural success, and the primary THV performance endpoint.

1-YEAR OUTCOMES. At 1 year follow-up (median 1.0 year; interquartile range: 1.0 to 1.2 years), 76.7% of the patients (23 of 30) were alive, and 84.2% were in New York Heart Association functional class I or II. A total of 5 deaths occurred between 30-day and 1-year follow-up; all were adjudicated as noncardiovascular. A descriptive summary of each patient, including essential baseline characteristics and outcomes, is provided in **Table 6**. A total of 5 patients had rehospitalizations for heart failure, 2 of them attributed to pre-existing underlying systolic or diastolic heart failure, 1 suspected to be secondary to paravalvular leak treated with percutaneous paravalvular leak closure, and 2 with suspected contribution from left-to-right shunts who underwent percutaneous closure of the iatrogenic interatrial septal defect. Additional adverse events were rare. There were no strokes after 30 days. Two patients were found to have hemolytic anemia after 30 days and were treated conservatively. There were no late migration or embolization events, THV thrombosis, or endocarditis. Patients who were alive at 1 year experienced significant improvement in New York heart Association functional class and in 6-min walk distance (**Central Illustration**), as well as quality-of-life scores (**Figure 4**). Most patients continued oral anticoagulation (**Figure 5**). The vast majority (70%) had atrial fibrillation at baseline as the main indication for long-term anticoagulation. Because of unknown risk for THV thrombosis, the investigators elected to continue anticoagulation in the remaining patients if no bleeding complications were present. Left ventricular function remained unchanged. TMVR device function remained stable with a median mean MVG of 6.0 mm Hg (interquartile range: 4.7 to 7.3 mm Hg) in the entire cohort, but mean MVG tended to be greater with the smaller 23-mm THVs (median 9.3 mm Hg; IQR: 6.0 to 14.5 mm Hg) (**Figure 6**). However, the high gradient in this group was driven by 1 patient treated with a 23-mm THV in a rigid ring (26-mm ET Logix) who had a mean MVG of 20 mm Hg at 30 days and 1 year. All patients had 1+ or less total MR at 1 year.

TABLE 5 Echocardiographic Characteristics at 30 Days and 1 Year

	30 Days* (n = 28)	1 Year† (n = 19)
Ejection fraction (%)	48.3 (39.1–52.2)	40.0 (32.7–57.5)
Stroke volume (ml)	68.2 (52.2–95.7)	75.9 (66.3–85.5)
Cardiac output (l/min)	5.0 (3.7–6.9)	5.0 (3.8–5.4)
Mean MVG (mm Hg)	7.6 (5.9–9.1)	6.0 (4.7–7.3)
MVA (cm^2)‡	2.1 (1.8–2.6)	2.4 (1.8–2.9)
Pulmonary artery systolic pressure (mm Hg)	44.4 (42.7–56.7)§	37.6 (33.4–52.5)‖
Peak LVOT gradient	4.6 (2.9–6.7)	4.3 (2.5–5.2)
Mean LVOT gradient	2.7 (1.6–3.7)	2.1 (1.4–3.1)
Severity of total mitral regurgitation		
None to trace	22/28 (77.7)	11/19 (57.9)
1 (+)	6/28 (22.2)	8/19 (42.1)
2 (+)	0/28 (0)	0 (0)
≥3 (+)	0/28 (0)	0 (0)
Severity of paravalvular mitral regurgitation		
None to trace	23/28 (81.5)	17/19 (89.5)
1 (+)	5/28 (18.5)	2/19 (10.5)
2 (+)	0/28 (0)	0/19 (0)
≥3 (+)	0/28 (0)	0/19 (0)

Values are median (interquartile range) or n/N (%). *2 died within 30 days. †7 died, 1 lost to follow-up, and 3 alive at 1 yr but missed 1-yr follow-up echocardiography. ‡Uncertain reliability; standard echocardiographic methods are validated in rheumatic disease and not mitral annular calcification or after transcatheter mitral valve replacement. §5 missing values. ‖3 missing values.

Abbreviations as in **Table 2**.

DISCUSSION

This is the first prospective, multicenter, early feasibility clinical trial with independent imaging core laboratories and independent clinical event adjudication to evaluate the safety and feasibility of transseptal MViR using the SAPIEN 3 balloon-expandable aortic THV. The following were the main findings: 1) transseptal MViR in carefully selected patients was associated with 30-day mortality lower than predicted by the Society of Thoracic Surgeons score; 2) transseptal MViR was associated with significantly reduced symptoms, improved 6-min walk distance, and improved quality-of-life scores; 3) THV performance was acceptable and remained stable in survivors at 1 year; 4) in this high-risk patient cohort, mortality at 1 year was similar to the reported mortality after transcatheter MV repair with the MitraClip or TMVR with THVs designed for the MV.

Our results differ from those of prior retrospective studies that evaluated the early experience of MViR procedures and demonstrated higher rates of procedure-related complications and mortality. The initial 30-day mortality rate in the VIVID registry was 11.4% in a patient population with a Society of Thoracic Surgeons score of 11% (2). A recent report from the same registry revealed a lower 30-day mortality rate of 8.5%, but the Society of Thoracic Surgeons score of these patients was also lower (7.4%) (11). Similarly, the initial 30-day mortality in the TVT Registry was 11.5% (3). These retrospective studies evaluated outcomes using first- and second-generation devices, and transapical access was used in a large proportion of these patients (50.7% and 35.8%, respectively) (3,11). With careful patient selection, the use of a third-generation device, and transseptal access in all cases, we found a 30-day mortality rate of 6.7% in a patient population with a median Society of Thoracic Surgeons score of 7.6%.

TABLE 6 Summary of Individual Patient Data

Patient #	Sex	Age (yrs)	Surgical Ring Brand	Ring Size (mm)	Pathology (MR, MS, Mixed)	SAPIEN 3 Size Recommended by MViV App	Mitral Annular Area by CT	SAPIEN 3 Size Chosen
1	F	86	St. Jude Tailor Band	29	MS	29	522	26
2	M	74	Edwards Classic	28	MS	23	386	23
3	M	64	Edwards ET Logix	28	MS	26	396	23
4	M	66	St. Jude Seguin	28	MR	26	610	26
5	M	77	Medtronic CG Future Band	34	MS	29	607	29
6	F	67	Medtronic CG Future Ring	30	MR	26	542	26
7	M	71	Edwards Classic	28	MR	23	357	26
8	M	78	Edwards Classic	30	MR	26	494	26
9	F	69	Edwards Physio (number not specified)	30	Mixed	26	496	26
10	M	67	Medtronic Simulus SemiRigid	28	MR	23/26	485	26
11	F	56	Edwards Physio	28	Mixed	26	444	26
12	M	72	Duran AnCore	29	MS	NA	434	26
13	M	83	Edwards Classic	30	MR	26	461	26
14	M	70	Edwards Physio 1 (4450)	30	Mixed	26	511	26
15	M	76	Medtronic GC Future Ring	36	MR	29	695	29
16	F	74	Physio I	28	MS	26	455	26
17	M	92	Physio II	26	MR	23	354	23
18	M	60	Sorin Memo 3D	28	MS	26	410	26
19	F	55	Physio	26	MS	23	381	23
20	M	58	Cosgrove band	28	MR	29	365	29
21	M	74	St. Jude Seguin	30	MR	26	533	29
22	F	70	Physio	26	MS	23	358	23
23	F	69	Physio 1	26	MR	23	362	23
24	F	82	Physio	28	MR	26	455	26
25	M	63	Medtronic CG Future Band	32	MR	26/29	735	29
26	M	74	Medtronic CG Future Ring	30	MR	26	521	29
27	M	74	Carbomedics Sorin Annuloflex	28	MS	23	503	29
28	M	79	Physio I	30	MR	26	394	26
29	F	67	Seguin	28	MR	26	477	26
30	F	84	Physio II	32	MR	29	590	29

CT = computed tomography; ICH = intracranial hemorrhage; MR = mitral regurgitation; MS = mitral stenosis; MVG = mitral valve gradient; MViV = mitral valve-in-valve; MVR = mitral valve replacement; NA = not available; PVL = paravalvular leak; THV = transcatheter heart valve.

Continued on the next page

The improved mortality was achieved with meticulous evaluation of the anatomy using cardiac CT imaging to determine suitability for MViR (12). The cardiac CT analysis helped us identify patients at risk for complications such as device embolization and LVOT obstruction, who were not accepted into the trial. Cardiac CT imaging was also used for preprocedural planning (7). Unlike retrospective registries, this selection process led to a very low rate of procedure-related complications. There were no intraprocedural deaths, THV device embolization, LVOT obstruction, or conversion to open heart surgery events during the index procedure.

The technical success rate was low (66.7%). This was driven primarily by the need for a second valve in 6 patients during the index procedure to treat MR resulting from a too atrial position of the THV. There were no adverse clinical consequences in these 6 patients. All of them were alive at 30 days and met the criteria for device success, procedural success, and the primary THV performance endpoint. The long-term effects of requirement for second valve are not known. Three of these patients had noncardiovascular death at 1 year, 1 was alive at 1 year but did not undergo echocardiography, and the other 2 were alive and met the primary THV performance endpoint by echocardiography at 1 year.

MORTALITY AND HOSPITALIZATION FOR HEART FAILURE AT 1 YEAR. The mortality rate at 1 year was 23.3%, which compares favorably with the 25.8%

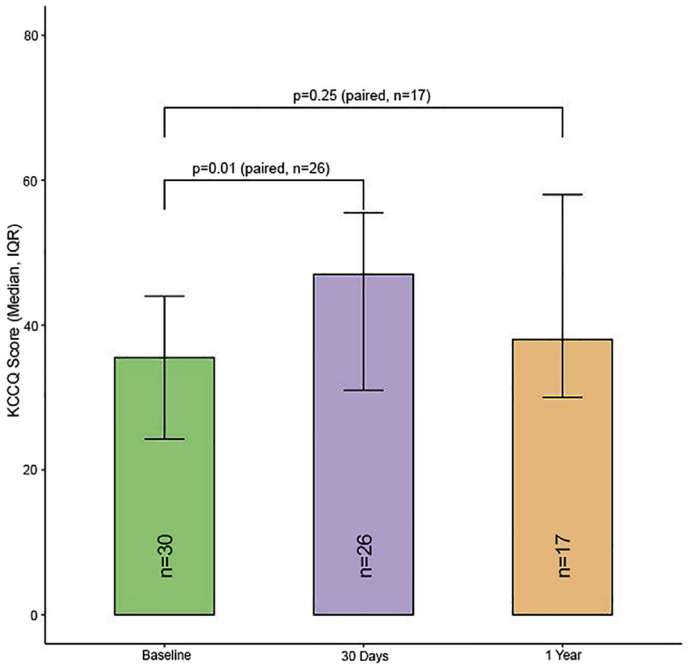
TABLE 6 Continued

Patient #	Technical Success	Need for Second Valve or Other Reason for No Technical Success	Alive at 30 Days	Procedural Success	THV Performance Endpoint Met at 30 Days	Alive at 1 Year	THV Performance Endpoint Met at 1 Year
1	No	Yes	Yes	Yes	Yes	No	NA (died prior to 1 yr)
2	No	Yes	Yes	Yes	Yes	No	NA (died prior to 1 yr)
3	Yes	No	Yes	No (mean MVG 10 mm Hg)	No (mean MVG 10 mm Hg)	Yes	No (mean MVG 10 mm Hg)
4	Yes	No	Yes	Yes	Yes	Yes	Yes
5	No	Yes	Yes	Yes	Yes	Yes	Alive at 1 yr but missed 1-yr visit
6	Yes	No	Yes	No (ICH)	Yes	Yes	Alive at 1 yr but missed 1-yr visit
7	Yes	No	Yes	No (mean MVG 10 mm Hg)	No (mean MVG 10 mm Hg)	Yes	Yes
8	Yes	No	Yes	Yes	Yes	Yes	Yes
9	Yes	No	Yes	Yes	Yes	Yes	Yes
10	No	No (PVL closure)	No	No (THV migration required MViV)	NA (died)	No	NA (died prior to 1 yr)
11	Yes	No	Yes	Yes	Yes	Yes	Yes
12	Yes	No	Yes	Yes	Yes	Yes	Yes
13	No	No, 2 (+) MR	No	No (died)	NA (died)	No	NA (died prior to 1 yr)
14	Yes	No	Yes	Yes	Yes	Yes	Yes
15	No	No, 2 (+) MR	Yes	Yes	Yes	Yes	Yes
16	Yes	No	Yes	Yes	Yes	Yes	Alive at 1 yr but missed 1-yr visit
17	Yes	No	Yes	No (mean MVG 10 mm Hg)	No (mean MVG 10 mm Hg)	No	NA (died prior to 1 yr)
18	No	No, 2 (+) MR and PVL closure	Yes	No (mean MVG 10 mm Hg)	No (mean MVG 10 mm Hg)	No	NA (died prior to 1 yr)
19	Yes	No	Yes	Yes	Yes	Yes	Yes
20	Yes	No	Yes	Yes	Yes	Yes	Yes
21	Yes	No	Yes	Yes	Yes	Yes	Yes
22	Yes	No	Yes	Yes	Yes	Yes	Yes
23	Yes	No	Yes	Yes	Yes	Yes	No (mean MVG 10 mm Hg)
24	Yes	No	Yes	Yes	Yes	Yes	Yes
25	No	Yes	Yes	Yes	Yes	Yes	Yes
26	Yes	No	Yes	No (hemolysis, surgical MVR)	Yes	Yes	NA (lost to follow-up)
27	Yes	No	Yes	Yes	Yes	Yes	Yes
28	No	Yes	Yes	Yes	Yes	Yes	Yes
29	Yes	No	Yes	Yes	Yes	Yes	Yes
30	No	Yes	Yes	Yes	Yes	No	NA (died prior to 1 yr)

1-year morality rate among patients treated with transcatheter MV edge to edge repair with the MitraClip in the United States (primary MR, 24.7%; secondary MR, 31.2%) (13). Similarly, the mortality observed in our study compares favorably with outcomes of TMVR studies evaluating THVs designed for the MV. The 30-day (6.7%) and 1-year (23.3%) all-cause mortality rates of transseptal MViR in this study were similar to or lower than the 30-day (6%) and 1-year (26%) mortality rates reported for the initial feasibility study of the Tendyne transcatheter valve system (Abbott Structural Heart, Santa Clara, California) (14) and similar to or lower than the initial experience with the Intrepid TMVR system (Medtronic, Redwood City, California), which showed a 30-day mortality rate of 14% and a 1-year mortality rate of 23.8% (15). Achieving 1-year mortality similar to that shown for a well-established and safe procedure such as transcatheter edge-to-edge MV repair or early experience with TMVR is encouraging and demonstrates this to be a treatment option for carefully selected patients.

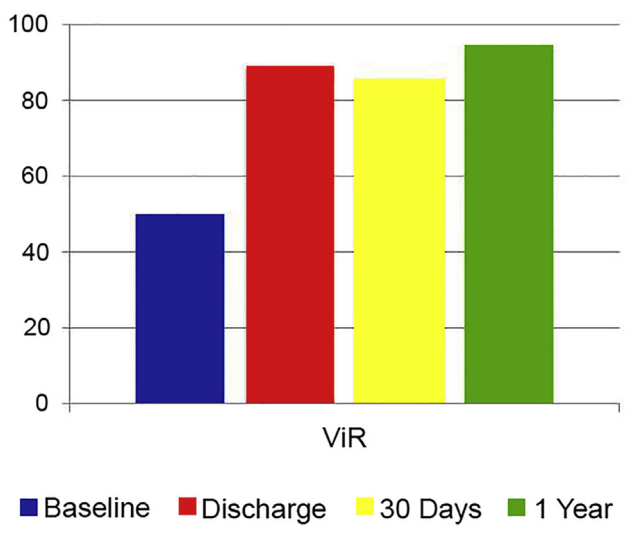
The composite rate of death or hospitalization for heart failure at 1 year of 40% was comparable with the 37.9% rate observed after MitraClip implantation in the United States and lower than the 51.3% observed

FIGURE 4 Quality-of-Life Scores



Error bars represent interquartile range (IQR). KCCQ = Kansas City Cardiomyopathy Questionnaire.

FIGURE 5 Percentage of Patients Receiving Oral Anticoagulation



ViR = valve-in-ring.

rate in the control arm of MITRA-FR (Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral Regurgitation) trial (13,16).

THV PERFORMANCE ENDPOINT. The primary THV performance endpoint of absence of MR grade 2+ or greater or mean MVG ≥10 mm Hg was achieved in 89.5% of patients alive with echocardiographic data available at 1 year (17 of 19). This finding is encouraging considering the round shape of the aortic THV and the variety of different shapes of surgical rings, with some of them being incomplete, as well as the different degrees of rigidity, which could result in higher rates of device migration or residual paravalvular leak. However, we excluded rigid rings after 1 rigid ring resulted in a high residual gradient early in this experience. It is important to avoid rigid rings in these procedures, as they can be associated with high residual gradients and a greater degree of paravalvular leak at commissures.

It is possible that a significant survivorship bias is present, as patients who died prior to 1-year follow-up could have had poorer THV performance. Although 3 of the 5 patients who died between 30 days and 1 year met the THV performance endpoint at 30 days, it is unknown if they developed MR or stenosis prior to their deaths.

Although the mean MVG was higher than reported for THVs designed for the mitral position (6.9 ± 4.0 mm Hg vs. 3.0 ± 1.1 mm Hg) (14), it was similar to the 6.5 ± 3.1 mm Hg gradient seen at 1 year in the VIVID registry (11). However, gradients tended to be higher with smaller size (23-mm) THVs, particularly in a rigid ring. The higher gradient likely reflects an element of patient-prosthesis mismatch inherent to placement of transcatheter valves in relatively undersized annuloplasty rings.

SPECIAL ANATOMIC CONSIDERATIONS. MViR is not ideal in rigid rings, as they could cause underexpansion of the THV, leading to higher residual MVGs as observed in the 1 rigid ring treated with a small THV in this study. Similarly, incomplete flexible rings are not ideal, because of higher risk for THV embolization, unless there is significant calcification and/or stenosis as underlying pathology, which could help anchor the THV. In general, we believe that rigid rings should be avoided, particularly when a small THV is needed.

STUDY LIMITATIONS. This was an early feasibility study with a small number of patients enrolled. Because it was not randomized and controlled, the results cannot provide evidence that MV intervention

in patients with failed surgical repair is associated with decreased mortality. In addition, it is possible that survivorship bias may have contributed to high rates of patients' meeting criteria for adequate THV performance at 1 year. Last, the patient population in our study was highly selected. Although the screen failure rate for cases presented in case-review conference calls was only 16.7%, it is possible that the real screen failure rates at individual sites were greater prior to case presentation. The participating investigators are highly experienced; it is possible that they elected not to present patients with rigid rings at risk for THV underexpansion causing residual gradients or incomplete bands at risk for THV embolization. Therefore, our results cannot be applied to the general population and do not support the widespread application of these procedures. Careful patient selection is essential to reproduce the results presented herein. Furthermore, MViR procedures have not been approved by the U.S. Food and Drug Administration and remain "off label" in the United States.

CONCLUSIONS

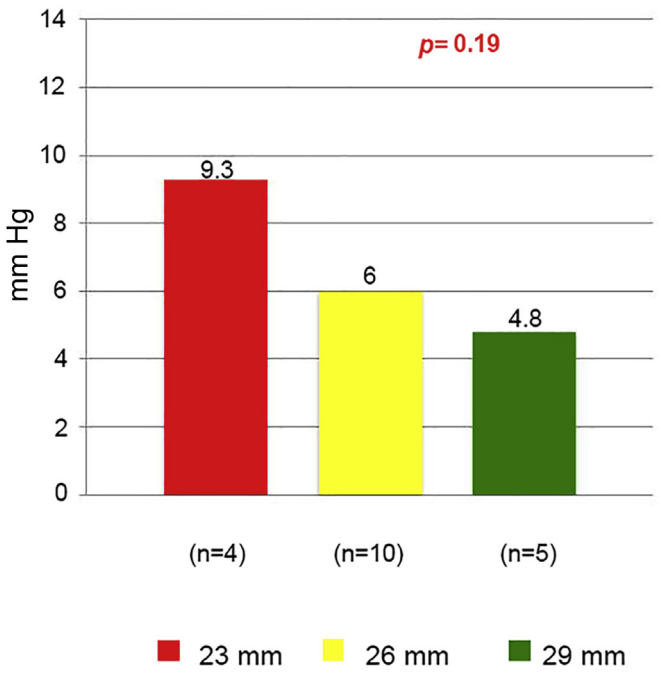
In patients at high surgical risk, transseptal MViR was associated with a 30-day mortality rate lower than predicted by the Society of Thoracic Surgeons score. At 1 year, transseptal MViR was associated with symptom alleviation and stable THV performance.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This study was supported by an unrestricted research grant from Edwards Lifesciences. The authors had absolute control of the study design, data collection, analysis and interpretation of data, writing of this paper, and take full responsibility for this report. Dr. Guerrero has received research grant support from Abbott Vascular and Edwards Lifesciences. Dr. Wang has served as a consultant for Edwards Lifesciences, Boston Scientific, Materialise, and HighLife Medical; and has received grant support from Boston Scientific. Dr. Salinger has served as a proctor for Boston Scientific and Edwards Lifesciences. Dr. Kodali has served as a consultant for Admedus, Meril Lifesciences, Abbott Vascular, JenaValve, and Claret Medical; and has ownership interest in Dura Biotech, Thubrikar Aortic Valve, Microinterventional Devices, and Supira Medical. Dr. Meduri has served as a consultant for Medtronic and Boston Scientific; and has served on the advisory board for Boston Scientific. Dr. Reisman has served as consultant for Edwards Lifesciences. Dr. Hahn has received speaker fees from Baylis Medical, Edwards Lifesciences, and Medtronic; is a consultant for Abbott Structural, Edwards Lifesciences, W.L. Gore & Associates, Medtronic, Navigate, and Philips Healthcare; has received nonfinancial support from 3mensio; holds equity in Navigate; and is the chief scientific officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she receives no direct industry compensation. Dr. Feldman is an employee of Edwards Lifesciences. Dr. O'Neill has served as consultant for Abiomed, Boston Scientific, and Edwards Lifesciences. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Mayra Guerrero, Mayo Clinic College of Medicine, Department of Cardiovascular Medicine, Mayo Clinic Hospital, 1216 2nd Street SW, Rochester, Minnesota 55905, USA. E-mail: mayraguerrero@icloud.com.

FIGURE 6 Mean Mitral Valve Gradient at 1 Year Follow-Up According to Transcatheter Heart Valve Size



PERSPECTIVES

WHAT IS KNOWN? Repeat MV surgery is associated with higher mortality than the risk associated with a first mitral operation.

WHAT IS NEW? Transseptal MViR in patients at high surgical risk with symptomatic MV disease due to failed surgical repair with an annuloplasty ring was associated with a 30-day mortality rate lower than predicted by the Society of Thoracic Surgeons score. At 1 year, patients experienced sustained reduction of symptoms and stable THV performance.

WHAT IS NEXT? Further studies are needed to refine the screening process to further improve patient selection and procedural results and to evaluate the long-term outcomes of these procedures.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 8, 2021
APRIL 26, 2021:846–58

REFERENCES

1. Mehaffey HJ, Hawkins RB, Schubert S, et al. Contemporary outcomes in reoperative mitral valve surgery. Heart 2018;104:652–6.

2. Dvir D. Transcatheter mitral valve-in-valve/valve-in-ring. Available at: https://www.tctmd.com/slide/tav-mitral-surgical-valves-and-rings-lessons-vivid-registry. Accessed August 27, 2018.

3. Guerrero M, Vemulapalli S, Xiang Q, et al. Thirty-day outcomes of transcatheter mitral valve replacement for degenerated mitral bioprostheses (valve-in-valve), failed surgical rings (valve-in-ring), and native valve with severe mitral annular calcification (valve-in-mitral annular calcification) in the United States: data from the Society of Thoracic Surgeons/American College of Cardiology/Transcatheter Valve Therapy Registry. Circ Cardiovasc Interv 2020;13:e008425.

4. Douglas PS, DeCara JM, Devereux RB, et al. Echocardiographic imaging in clinical trials: American Society of Echocardiography standards for echocardiography core laboratories: endorsed by the American College of Cardiology Foundation. J Am Soc Echocardiogr 2009;22:755–65.

5. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2017;30:303–71.

6. Achenbach S, Delgado V, Hausleiter J, Schoenhagen P, Min JK, Leipsic JA. SCCT expert consensus document on computed tomography imaging before transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR). J Cardiovasc Comput Tomogr 2012;6:366–80.

7. Guerrero M, Salinger M, Pursnani A, et al. Transseptal transcatheter mitral valve-in-valve: a step by step guide from preprocedural planning to postprocedural care. Catheter Cardiovasc Interv 2018;92:E185–96.

8. Bapat V. Valve-in-valve apps: why and how they were developed and how to use them. EuroIntervention 2014;10 suppl U:U44–51.

9. Guerrero M, Wang DD, Pursnani A, et al. A cardiac computed tomography-based score to categorize mitral annular calcification severity and predict valve embolization. J Am Coll Cardiol Img 2020;13:1945–57.

10. Al-Hijji MA, El Sabbagh A, Guerrero ME, Rihal CS, Eleid MF. Paravalvular leak repair after balloon-expandable transcatheter mitral valve implantation in mitral annular calcification: Early experience and lessons learned. Catheter Cardiovasc Interv 2019;94:764–72.

11. Simonato M, Whisenant B, Barbosa Ribeiro H, et al. Transcatheter mitral valve replacement after surgical repair or replacement: comprehensive midterm evaluation of valve-in-valve and valve-in-ring implantation from the VIVID registry. Circulation 2021;143:104–16.

12. Wang DD, Eng MH, Greenbaum AB, et al. Validating a prediction modeling tool for left ventricular outflow tract (LVOT) obstruction after transcatheter mitral valve replacement (TMVR). Catheter Cardiovasc Interv 2018;92:379–87.

13. Sorajja P, Vemulapalli S, Feldman T, et al. Outcomes with transcatheter mitral valve repair in the United States: an STS/ACC TVT Registry report. J Am Coll Cardiol 2017;70:2315–27.

14. Sorajja P, Moat N, Badhwar V, et al. Initial feasibility study of a new transcatheter mitral prosthesis: the first 100 patients. J Am Coll Cardiol 2019;73:1250–60.

15. Bapat V, Rajagopal V, Meduri C, et al. Early experience with new transcatheter mitral valve replacement. J Am Coll Cardiol 2018;71:12–21.

16. Obadia JF, Messika-Zeitoun D, Leurent G, et al. Percutaneous repair or medical treatment for secondary mitral regurgitation. N Engl J Med 2018;379:2297–306.

KEY WORDS mitral valve-in-ring, surgical mitral valve repair, transcatheter mitral valve replacement

APPENDIX For inclusion and exclusion criteria, trial operations, supplemental methods, study endpoints, and supplemental references, please see the online version of this paper.