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ORIGINAL RESEARCH

STRUCTURAL

6-Month Outcomes of a Supra-Annular Transcatheter Mitral Valve Replacement

An Early Feasibility Study

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ABSTRACT

BACKGROUND The AltaValve transcatheter mitral valve replacement (TMVR) system is an atrial fixation TMVR device that is designed to overcome the limitations of transcatheter edge-to-edge repair and current TMVR devices.

OBJECTIVES The aim of this study was to evaluate the procedural feasibility, safety, and performance of the AltaValve system in treating patients with symptomatic mitral regurgitation (MR) and unsuitable for surgery.

METHODS The primary endpoint of the AltaValve Early Feasibility Study was technical success, defined as: 1) absence of procedural mortality; 2) successful delivery and deployment of the implant; 3) successful retrieval of the delivery system; and 4) no emergency surgery or re-intervention related to the implant. Echocardiographic data were assessed by an independent core laboratory, while all reported events were adjudicated by an independent clinical events committee.

RESULTS A total of 30 patients with a median age of 77 years were enrolled. Median follow-up duration was 182 days (Q1-Q3: 171-191 days). Procedural success was achieved in 29 of the 30 cases (96.7%; 95% CI: 82.8%-99.9%). Reduction to mild or less MR was achieved in all surviving patients at 30 days and maintained in all but 1 patient at 6 months. There were no strokes, new pacemaker implantations, or mitral valve reinterventions within 6 months postprocedure. Significant improvements were observed in functional class and quality-of-life assessments.

CONCLUSIONS Among patients with significant MR, the AltaValve TMVR system was feasible, safe, and associated with good valve function at 6 months. (AltaValve Early Feasibility Study Protocol; NCT03997305).
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Over the past decade, transcatheter mitral valve replacement (TMVR) devices have attempted to become an alternative for patients with mitral valve disease ineligible for surgery or transcatheter edge-to-edge repair (TEER).[1-9] As opposed to transcatheter aortic valve replacement, TEER, or even transcatheter tricuspid valve replacement, TMVR has struggled, and to date, no TMVR platforms are commercially approved for clinical use in the United States, and only the Tendyne (Abbott Vascular) transapical system is approved in Europe. Most TMVR devices rely on complex subvalvular fixation, which is associated with increased risk for left ventricular outflow tract (LVOT) obstruction, and are limited by anatomical variability in mitral annular dimensions and the presence of calcification.[10] Previous studies have reported screening failure rates for TMVR up to 80%, with the most frequent reasons being mitral valve annular size, presence of significant mitral annular calcification, and risk for LVOT obstruction.[11-13]

The AltaValve system (4C Medical Technologies) is a novel TMVR device that uses an atrial fixation approach designed to avoid the mitral annulus and subvalvular apparatus for anchoring, therefore minimizing the risk for LVOT obstruction.[14-16] The AltaValve EFS (Early Feasibility Study) was conducted to assess the procedural feasibility, preliminary safety, and performance of the AltaValve system in treating patients with symptomatic mitral regurgitation (MR). Here we present data from 30 patients with MR ≥3+ enrolled in the AltaValve EFS and their 6-month clinical and echocardiographic outcomes.

METHODS

STUDY DESIGN. The AltaValve EFS (NCT03997305) is a prospective, single-arm, multicenter study conducted to evaluate the safety and performance of the AltaValve for the treatment of severe MR in subjects who were considered high risk for conventional open heart surgery and were not suitable for mitral valve TEER. Twelve sites in the United States and Europe enrolled patients (Supplemental Table 1). Applicable regulatory authorities approved the study in each participating country and center, and all patients were consented prior to the procedures. The study adhered to Good Clinical Practice guidelines and was conducted in accordance with the Declaration of Helsinki. As this was an early feasibility study designed to collect initial data on safety and performance, the sample size was based on regulatory and logistical considerations and not a formal power calculation for a statistical hypothesis test.

PATIENT POPULATION. All patients presented with moderate to severe or severe MR (≥3+), were determined to be at high surgical risk by the local heart team, and had symptoms of heart failure (NYHA functional class ≥II). Exclusion criteria included severe left ventricular dysfunction (ejection fraction <30%), severe pulmonary hypertension (systolic pressure >70 mm Hg), advanced kidney dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m^2), and severe tricuspid regurgitation. A complete list of inclusion and exclusion criteria is presented in Supplemental Table 2. Patients underwent transthoracic and transesophageal echocardiography for assessment of MR severity and etiology.

AltaValve TMVR SYSTEM AND PROCEDURE. The AltaValve (**Central Illustration**, Supplemental Figure 1) comprises a self-expanding Nitinol stent frame that houses a 27-mm trileaflet bovine pericardial valve.[17] A fabric skirt surrounds the lower portion of the stent, termed the annular ring, to seal around the mitral valve and minimize paravalvular leakage. Three sizes of annular ring are available: 40, 46, and 54 mm. The outer frame is oversized relative to each patient's left atrial height and width to ensure proper anchoring. Preprocedural planning involves analysis using both computed tomography and transthoracic echocardiography. Transesophageal echocardiography was not required for AltaValve screening.

Although the device was originally delivered using a transapical (TA) approach (**Figures 1A to 1C**), a transseptal (TS) approach (**Figures 1D to 1G**) was developed and represents the major current delivery mode. The TS approach procedure is performed via percutaneous femoral venous access followed by standard TS puncture, followed by balloon septostomy (an 8- to 10-mm balloon is recommended). A guide and dilator are tracked into left atrium over a guidewire under transesophageal echocardiographic guidance. Next, the dilator is removed, and a 29-F delivery catheter (with preloaded implant) is navigated to approximately 10 to 15 mm below the mitral valve annulus, and implant deployment is initiated. There are 2 critical steps for AltaValve deployment: 1) because the AltaValve has a small left ventricular profile, lateral engagement is critical at initial implant deployment to ensure in-sync movement of the AltaValve's annular ring with the native mitral valve

ABBREVIATIONS AND ACRONYMS

6MWD = 6-minute walk distance

ASD = atrial septal defect

KCCQ = Kansas City Cardiomyopathy Questionnaire

LVOT = left ventricular outflow tract

MR = mitral regurgitation

TA = transapical

TS = transseptal

TEER = transcatheter edge-to-edge repair

TMVR = transcatheter mitral valve replacement

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CENTRAL ILLUSTRATION **AltaValve Early Feasibility Study**

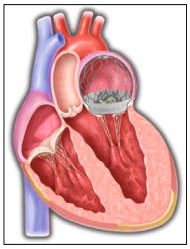
6-Month Outcomes of a Supra-Annular Transcatheter Mitral Valve Replacement: The AltaValve Early Feasibility Study, N = 30

Patients Characteristics

- 30 Patients with ≥3+ MR, high risk for surgery, and not candidates for mitral TEER
- Median age 77 years
- 63% Female
- 50% Functional MR, 43% degenerative MR, and 7% mixed MR etiology
- MAC present in 26.7% (8/30)

Study Characteristics

- AltaValve bioprosthesis uses an atrial anchoring mechanism with a self-expandable large opened cell nitinol cage
- 13 Transapical and 17 transseptal access
- Median follow-up 182 days



Primary Endpoints

- Technical success: 96.7% (29/30)
- All-cause mortality at 30 days: 10.3% (3/29)

6-Month Outcomes

Death	**13.8% (4/29)**
Cardiac death	6.9% (2/29)
Stroke	0% (0/29)
HF hospitalization	13.8% (4/29)
Mitral regurgitation	
None/trivial	78.3% (18/23)
Mild	17.4% (4/23)
Moderate	4.3% (1/23)
Moderate to severe	0%
Severe	0%

- Technical success was achieved in 97% and 30-day mortality was 10%.
- Reduction to mild or less MR was achieved in all survivng patients at 30 days and maintained in all but 1 patient at 6 months.
- No strokes, new pacemaker implantations, or MV re-interventions within 6 months after the procedure.
- By 6-month follow-up, significant improvements were observed in functional class and quality of life assessments.

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The AltaValve is a supra-annular mitral valve (MV) replacement bioprosthesis using an atrial anchoring mechanism with a self-expandable large open-cell Nitinol cage. The AltaVista Early Feasibility Study included 30 patients presenting with grade 3+ or 4+ mitral regurgitation (MR) deemed high risk for surgical valve replacement and not suitable for transcatheter edge-to-edge repair (TEER). The AltaValve was deployed via transapical access in 13 patients and transfemoral access in 17 patients. Mitral annular calcification (MAC) was present in 8 patients. Six-month outcomes demonstrated the safety and feasibility of the AltaValve for the treated population. HF = heart failure.

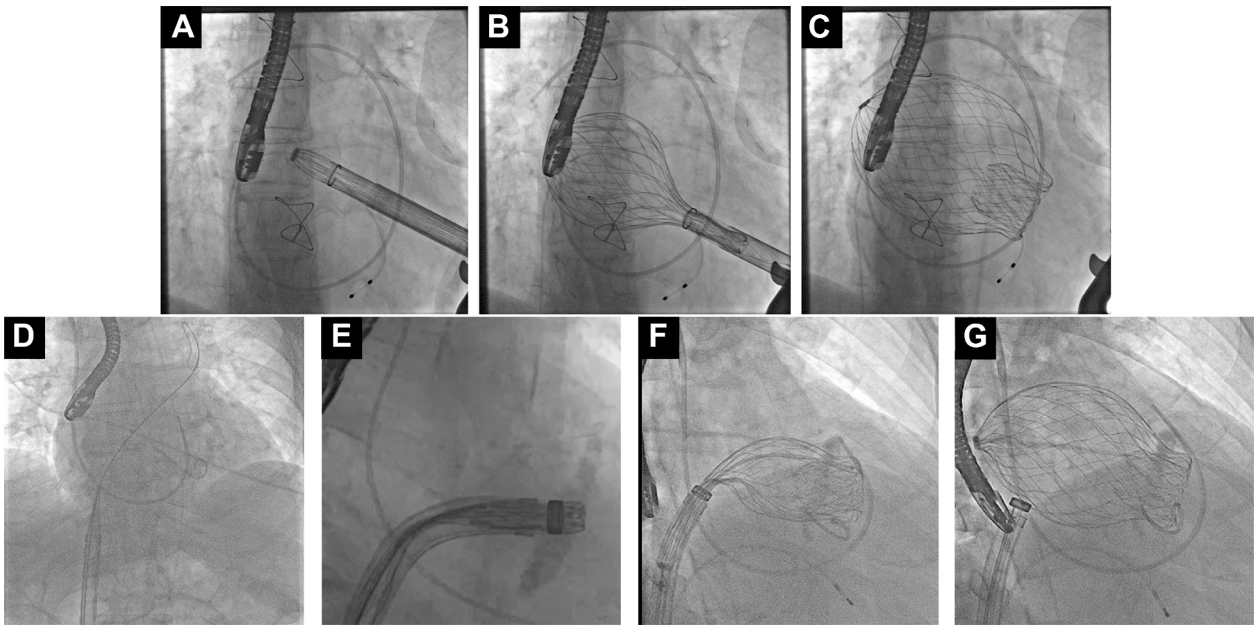
annulus; and 2) use of the positioner that allows the operator to maintain the annular ring at the targeted depth throughout deployment. After complete deployment, valve position and hemodynamic performance are assessed before positioner release and final disengagement of the implant from the delivery catheter. If needed, the AltaValve can be repositioned at any time throughout deployment, as long as the implant is still attached to the delivery catheter. Additionally, 40- and 46-mm annular ring implants can be fully recaptured, even after full deployment.

Following the AltaValve procedure, a 6-month course of anticoagulation therapy is recommended.

FOLLOW-UP. Patients are followed at 30 days, 6 months, 12 months, and yearly thereafter for 5 years. Each visit includes transthoracic echocardiography (Figures 2A and 2B), assessment of NYHA functional class, laboratory tests, a review of adverse events, 6-minute walk test, and Kansas City Cardiomyopathy Questionnaire (KCCQ) to assess quality of life. Echocardiographic data are assessed by an independent core laboratory (Cardiovascular Imaging Core Laboratory), and clinical events are adjudicated by an independent clinical events committee.

STUDY ENDPOINTS. The primary study endpoints included technical success measured at exit from the procedure room and all-cause mortality at 30 days. Technical success at completion of the procedure was defined as: 1) absence of procedural mortality; 2) successful delivery and deployment of the implant;

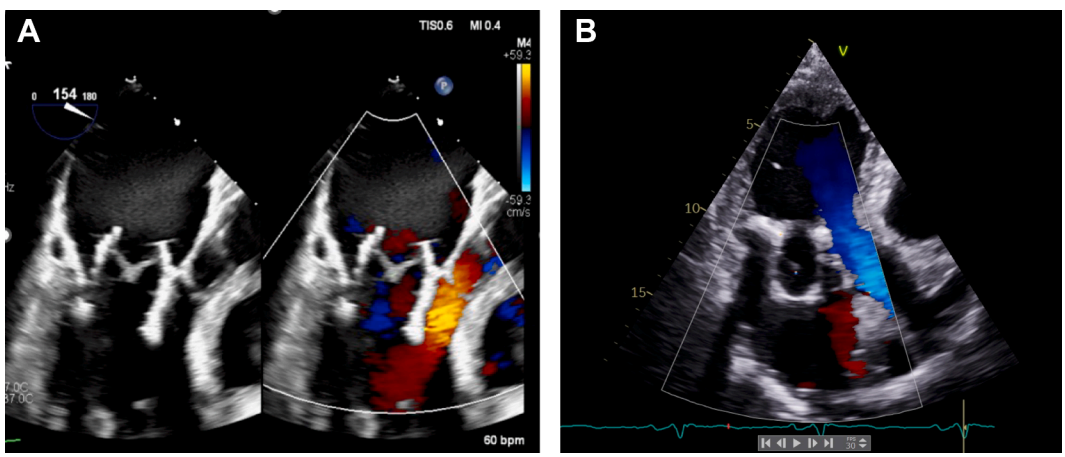
FIGURE 1 **AltaValve Deployment**



AltaValve deployment using transapical (A to C) and transseptal (D to G) delivery systems. (A) After transapical access, the delivery catheter is inserted into left atrium with the implant tip exposed. (B) AltaValve partially deployed. (C) AltaValve fully deployed. (D) Transseptal left atrial access with guide and dilator. (E) The AltaValve system is navigated to the mitral valve plane. (F) AltaValve partially deployed. (G) AltaValve fully deployed while the system is maintained in the left atrium.

3) successful retrieval of the delivery system; and 4) no emergency surgery or re-intervention related to the implant. Additional nonprespecified exploratory analyses include device performance assessment, defined as: 1) absence of MR grade ≥2+; and 2) valve gradient ≤10 mm Hg postprocedure. Secondary endpoints evaluated the incidence of clinical adverse events, including stroke, bleeding, myocardial infarction, hemolysis, endocarditis, re-intervention, recurrent heart failure, prolonged hospitalization, device embolization, LVOT obstruction, and cardiac electrical conduction disturbances.

FIGURE 2 **Postprocedure Echocardiogram of AltaValve**



(A) Transesophageal echocardiographic images immediately postprocedure. (B) Transthoracic echocardiography 6 months postprocedure.

TABLE 1 Baseline Characteristics (N = 30)

Age, y	77.0 ± 6.2 (30), 77.0 (61.0-85.0)
Female	63.3 (19/30)
Body mass index, kg/m^2	26.5 ± 4.1 (30), 26.2 (20.5-37.2)
Smokers (current or previous)	40.0 (12/30)
STS Predicted Risk of Mortality, %	5.3 ± 1.8 (30), 4.8 (1.6-8.3)
White/Caucasian	96.7 (29/30)
Hispanic/Latino	3.3 (1/30)
Black/African American	0.0 (0/30)
Asian	0.0 (0/30)
American Indian or Alaska Native	6.7 (2/30)[a]
Previous cardiac intervention	83.3 (25/30)
Prior coronary artery bypass surgery	23.3 (7/30)
Prior percutaneous coronary intervention	46.7 (14/30)
Prior valve procedure	20.0 (6/30)
Aortic valve procedure	16.7 (5/6)
Mitral valve procedure	3.3 (1/6)
Pulmonary valve procedure	0.0 (0/6)
Tricuspid valve procedure	0.0 (0/6)
NYHA functional class III/IV	80.0 (24/30)
Atrial fibrillation	76.7 (23/30)
Chronic (persistent or permanent)	52.2 (12/23)
Paroxysmal	47.8 (11/23)
Prior stroke	13.3 (4/30)
Prior transient ischemic attack	3.3 (1/30)
Chronic kidney disease[b]	43.3 (13/30)
Chronic obstructive pulmonary disease	16.7 (5/30)
Coronary artery disease	76.7 (23/30)
Diabetes mellitus	30.0 (9/30)
Prior heart failure (hospitalization)	26.7 (8/30)
Hypertension	93.3 (28/30)
Peripheral arterial disease	13.3 (4/30)
Prior myocardial infarction	30.0 (9/30)

Values are mean ± SD (n), median (Q1-Q3) or % (n/N). [a]Two patients reports both White/Caucasian and American Indian/Alaska Native races. [b]Chronic kidney disease was defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2.

STS = Society of Thoracic Surgeons.

STATISTICAL ANALYSIS. The analysis was preplanned to compare baseline, postprocedural, discharge, 30-day, and 6-month outcomes. Descriptive statistical analyses were performed, and the data are presented as mean ± SD, median (Q1-Q3), or frequency (percentage). Analyses were performed in Excel (Microsoft) or R version 4.3.2 (R Foundation for Statistical Computing).

RESULTS

From January 2023 to May 2024, 145 patients were screened from 12 sites. Among them, 95 (66%) were anatomically suitable for the study procedure. Among the 50 patients (44%) not anatomically suitable, 20 failed screening for left atrial dimension, 15 for left atrium dynamic volume change, 10 for mitral valve annular dimension, and 5 for other reasons. Among the 95 patients anatomically suitable for AltaValve, 65 were excluded for medical reasons such as lack of significant MR, significant frailty, mitral stenosis, severe tricuspid regurgitation, and severe pulmonary hypertension. Among the 30 patients enrolled, 13 (43.3%) were deemed not suitable for TEER by enrolling sites, confirmed by the study core laboratory. Reasons for not being suitable for TEER were a short posterior leaflet (defined as ≤7 mm; n = 13), multiple jets (n = 11), and leaflet calcification (n = 9).

Baseline characteristics are provided in Table 1. The mean age was 77.0 ± 6.2 years, and 63% of patients were women. Most patients (80%) were in NYHA functional class III or IV. Baseline echocardiography data are provided in Table 2. Most patients (80%) had severe MR, and 20% had moderate to severe MR. In terms of MR etiology, 50% had functional MR, 43% had degenerative MR, and 7% had mixed MR etiology. Left ventricular ejection fraction was ≤50% in 33.3% of patients. Mitral annular calcification was present in 8 patients (26.7%) (mild in 3 patients, moderate in 4 patients, and severe in 1 patient), with a mean volume of calcification of 238 mL.

PROCEDURAL CHARACTERISTICS AND OUTCOMES. Thirteen patients (43.3%) underwent implantation using a TA approach and 17 (56.7%) using a TS approach (Table 3). Technical success was achieved in 97% of cases (29 of 30). One of the first TS patients was converted to surgery during the index procedure. For this patient, the delivery system was damaged during a recapture and repositioning maneuver, precluding any further manipulation of the system. The decision was made to convert the patient to surgery. The patient died of surgical complications with multiorgan failure 4 days postprocedure. Two patients had complex mitral annular calcification for which balloon valvuloplasty (with the Inoue-Balloon, Toray) was used to predilate the mitral valve annulus prior to AltaValve placement, and both cases were completed successfully without procedural complications. Six patients (35.3% of the TS patients) required atrial septal defect closure during the index procedure because of bidirectional shunts. None of the implanted patients had LVOT obstructions postprocedure, and MR resolved to none or trace in 96.6% (28 of 29) and mild in 3.4% (1 of 29) postprocedure.

CLINICAL OUTCOMES. Thirty-day and 6-month clinical outcomes are reported in Table 4. Among 29

TABLE 2 Baseline Echocardiographic Parameters (N = 30)

Mitral valve pathology	
Degenerative	43.3 (13/30)
Functional	50.0 (15/30)
Mixed	6.7 (2/30)
Mitral regurgitation	
Moderate to severe	20.0 (6/30)
Severe	80.0 (24/30)
LVEF	
25%-50%	33.3 (10/30)
>50%	66.7 (20/30)
Aortic regurgitation	
None/trace	66.7 (20/30)
1+	30.0 (9/30)
2+	3.3 (1/30)
3+	0.0 (0/30)
Tricuspid regurgitation	
None/trace	3.3 (1/30)
1+	26.7 (8/30)
2+	66.7 (20/30)
3+	3.3 (1/30)

Values are % (n/N).
LVEF = left ventricular ejection fraction.

patients with implanted AltaValve devices, 3 deaths occurred prior to 30-day follow-up: 2 TA patients on day 2 and day 3 after the index procedure (attributed to the TA procedures) and 1 TS patient on day 26 of hospital-acquired infection. One additional TA patient exited prior to 6 months because of a mechanical fall. There were no strokes, new pacemaker implantations, or mitral valve reinterventions through 6 months (or thereafter reported in the study). There was significant improvement in NYHA functional class, with 92% subjects (24 of 26) improving to functional class II or I at 30 days. Reduction in NYHA functional class was maintained at 6 months, with 82% (19 of 23) reporting functional class II or I. Four patients reported NYHA functional class III at 6 months: 1 TA patient was hospitalized for a urinary tract infection and right heart failure hospitalization (also resulting in decreased KCCQ score and 6-minute walk distance [6MWD] from baseline); 1 TS patient noted limitation in the setting of severe tricuspid regurgitation, although KCCQ score and 6MWD improved from baseline; 1 TS patient noted limitation in the setting of severe tricuspid regurgitation, reported a decreased KCCQ score compared with baseline, and did not perform the 6-minute walk test; and 1 TS patient experienced gastrointestinal bleeding (also resulting in a decreased KCCQ score compared with baseline). Among the entire study cohort, the mean KCCQ score improved from 54.9 ± 20.9 at baseline (95% CI: 46.9-62.8) to 67.7 ± 21.7 (95% CI: 58.5-76.9) ($P = 0.033$) at 6-month follow-up. The mean KCCQ score for TS patients only improved from 54.2 ± 23.2 at baseline (95% CI: 41.8-66.5) to 69.9 ± 17.5 (95% CI: 60.2-79.6) ($P = 0.032$) at 6-month follow-up. Significant KCCQ score improvement (defined as improvement of at least 10 points) was demonstrated in 70% of patients (16 of 23) of the entire study cohort and 73% of TS patients (11 of 15) at 6 months. The 6MWD demonstrated improvement from 234 ± 98 m at baseline (95% CI: 197-271 m) to 294 ± 106 m (95% CI: 249-339 m) ($P = 0.025$) at 6 months for the entire cohort and from 220 ± 83 m at baseline (95% CI: 175-264 m) to 299 ± 109 m at 6 months (95% CI: 226-372 m) ($P = 0.004$) for TS patients.

TABLE 3 Procedural Characteristics and Outcomes (N = 30)

	% (n/N)	95% CI
Location of treatment		
United States	43.3 (13/30)	25.5-62.6
European Union	56.7 (17/30)	37.4-74.5
Procedural approach		
Transapical	43.3 (13/30)	25.5-62.6
Transseptal	56.7 (17/30)	37.4-74.5
Annular ring size		
40 mm	23.3 (7/30)	9.9-42.3
46 mm	50 (15/30)	31.3-68.7
54 mm	26.7 (8/30)	12.3-45.9
Conversion to sternotomy	3.3 (1/30)	0.0-17.2
Atrial septal defect closure	35.3 (6/17)	14.2-61.7
Technical success	96.7 (29/30)	82.8-99.9

Values are % (n/N).

30-DAY AND 6-MONTH ECHOCARDIOGRAPHIC OUTCOMES. Echocardiographic outcomes at 30 days and 6 months are listed in Table 5. At 30-day follow-up, 100% of patients had sustained MR improvement, with 92.3% (24 of 26) having no or trace MR and 7.7% having mild MR. This was maintained at 6 months, with 78.3% (18 of 23) having no or trace MR and 17.4% (4 of 23) having mild MR. One patient reported moderate MR at 6 months associated with gastrointestinal bleeding that was addressed, resulting in MR reduction. The mean mitral valve gradient was 4.1 ± 1.7 mm Hg at 30 days and maintained at 3.7 ± 1.0 mm Hg at 6 months. Left ventricular ejection fraction remained preserved in most patients throughout 6 months. There was no echocardiographic evidence of device displacement, fracture, migration, or embolization.

DISCUSSION

In the AltaValve EFS, we evaluated the safety and efficacy of the AltaValve device, a novel TMVR

TABLE 4 6-Month Clinical Outcomes Among Patients With AltaValve Implanted

			30 Days	95% CI	6 Months	95% CI
Adverse events						
All-cause mortality			10.3 (3/29)	2.2-27.4	13.8 (4/29)	3.9-31.7
Cardiac mortality			6.9 (2/29)	0.8-22.8	6.9 (2/29)	0.8-22.8
Stroke			0 (0/29)	0.0-11.9	0 (0/29)	0.0-11.9
Heart failure hospitalization			3.4 (1/29)	0.0-17.8	13.8 (4/29)	3.9-31.7
	Baseline (n = 29)	**95% CI**	**30 Days (n = 26)**	**95% CI**	**6 Months (n = 23)**	**95% CI**
NYHA functional class						
I	0 (0/29)	0.0-11.9	30.8 (8/26)	14.3-51.8	21.7 (5/23)	7.5-43.7
II	20.7 (6/29)	8.0-39.7	65.4 (17/26)	44.3-82.8	60.9 (14/23)	38.5-80.3
III	72.4 (21/29)	52.8-87.3	3.8 (1/26)	0.0-19.6	17.4 (4/23)	5.0-38.8
IV	6.9 (2/29)	0.8-22.8	0 (0/26)	0.0-13.2	0 (0/23)	0.0-14.8
KCCQ score	54.9 ± 20.9	46.9-62.8	59.7 ± 26.8	48.9-70.5	67.7 ± 21.7	58.5-76.9
Trans-septal approach	54.2 ± 23.2	41.8-66.5	64.9 ± 26.5	50.2-79.5	69.9 ± 17.5	60.2-79.6
6MWD, m	234. ± 97.9	197-271	251 ± 86.9[a]	216-286	294 ± 106[b]	249-339
Trans-septal approach	220 ± 83.3	175-264	250 ± 86.7	194-305	299 ± 109	226-372

Values are % (n/N) or mean ± SD. [a]Evaluable patients, n = 21 (5 patients did not complete assessment). [b]Evaluable patients, n = 18 (5 patients did not complete assessment).
6MWD = 6-minute walk distance; KCCQ = Kansas City Cardiomyopathy Questionnaire.

platform with a supra-annular fixation system. The main findings of this study are as follows: 1) the AltaValve TMVR system was feasible, safe, and associated with a high rate of technical success; 2) at 30 days and 6 months, most patients had complete resolution of MR with low transvalvular gradients and intended prosthetic valve function; and 3) there were no major adverse cardiac events, including need for re-intervention, LVOT obstruction, and embolization.

AltaValve implantation was safe, with no procedural death, prosthesis migration, or embolization. AltaValve's deployment is performed with a slow and controlled unsheathing of a self-expandable Nitinol device, with the possibility of full recapture if positioning is deemed not optimal. This is different from many other TMVR platforms, which use either a balloon-expandable platform or other subvalvular anchoring mechanisms, with no possibility of recapture or repositioning. The recapturability of the

TABLE 5 Echocardiographic Outcomes

	Baseline	Discharge	30 Days	6 Months
Mitral regurgitation				
None/trivial	0	96.2 (25/26)	92.3 (24/26)	78.3 (18/23)
Mild	0	3.8 (1/26)	7.7 (2/26)	17.4 (4/23)
Moderate	0	0	0	4.3 (1/23)
Moderate to severe	20 (6/30)	0	0	0
Severe	80 (24/30)	0	0	0
Mitral valve mean gradient, mm Hg	2.5 ± 1.4 (30)	3.4 ± 1.1 (25)	4.1 ± 1.7 (26)	3.7 ± 1.0 (23)
LVOT obstruction	N/A	0	0	0
LVOT gradient, mm Hg	1.3 (1-1.6)	2.6 (1.9-3.4)	1.9 (1.5-2.4)	1.6 (1.3-1.8)
LV end-diastolic diameter, cm	5.4 ± 0.7 (30)	5.0 ± 1.1 (26)	5.3 ± 0.8 (26)	5.3 ± 0.7 (23)
LV end-systolic diameter, cm	3.9 ± 0.9 (30)	3.9 ± 1.0 (26)	4.1 ± 1.0 (26)	4.0 ± 1.0 (23)
LV ejection fraction				
<25%	0	0	0	0
25%-50%	33.3 (10/30)	40.0 (10/25)	38.5 (10/26)	43.5 (10/23)
>50%	66.7 (20/30)	60.0 (15/25)	61.5 (16/26)	56.5 (13/23)
LV ejection fraction, %	53.8	51.5	51.6	52.6
LV stroke volume, mL	79.2	61.2	65.3	70.9
Moderate or greater tricuspid regurgitation	70 (21/30)	76 (19/25)	76 (19/25)	73.9 (17/23)
Right ventricular systolic pressure, mm Hg	44.4 ± 17.4 (21)	48.5 ± 8.6 (21)	47.3 ± 13.8 (20)	47.0 ± 12.8 (20)

Values are % (n/N), mean ± SD, or median (Q1-Q3).
LV = left ventricular; LVOT = left ventricular outflow tract.

AltaValve, paired with its "soft" implantation and deployment, most likely explained the excellent safety results of our study. This finding is important especially in comparison with other well-established transcatheter mitral valve repair therapies, such as TEER. Indeed, procedural safety and reproducibility will be key for device adoption and dissemination and in the future when potentially comparing AltaValve with more mature and proven techniques such as mitral TEER or even surgery.

AltaValve implantation was associated with no LVOT obstruction during the procedure or at 30 days. LVOT obstruction post-TMVR is known to be associated with high mortality and morbidity and, despite appropriate planning, still occurred in up to 13% of cases with other intra-annular TMVR platforms.[10,18-21] Predicted risk for LVOT obstruction is also one of the main reasons for screening failure among other TMVR studies.[13] Similarly, all patients enrolled in the AltaValve EFS were at high risk for surgery, and most were unsuitable for mitral valve TEER. Most of the patients included in our study also failed screening for clinical studies of other TMVR devices that rely on intra- or subannular anchoring. Given the known limitations of current TMVR platforms, the AltaValve TMVR device may expand the proportion of patients with severe MR who can be treated.

No safety issues were detected at 6-month follow-up with regard to stroke or arrythmia. Intuitively, the presence of a cage in the entire left atrium may legitimately raise concern for excess thrombogenicity, atrial arrythmia, or device fracture. However, no such complications were observed through 6 months (or at any time point thereafter). The AltaValve frame is composed of very thin and flexible struts with large cells, allowing rapid endothelialization, while conserving left atrial contractility. The majority of patients included in this study (and similar to the treated MR population in general) were in atrial fibrillation, with an indication for oral anticoagulation. Although many patients with AltaValve implants have more than 1-year follow-up with no arrhythmic or thromboembolic complications, longer follow-up is needed.

STUDY LIMITATIONS. These results represent the early outcomes of a small feasibility study and, therefore, have limited external validity. Long-term assessment of the study cohort is ongoing and will be reported upon study completion to thoroughly evaluate valve dynamics and clinical outcomes in the implanted patients. Most of the patients experienced significant improvements in quality of life as measured by NYHA functional class, KCCQ score, and 6MWD; however, because of the small number of patients, these results are only hypothesis generating. Larger prospective studies are necessary to further evaluate the safety and efficacy of the device.

CONCLUSIONS

The initial findings from the AltaValve EFS confirm the safety and efficacy of the AltaValve for patients with significant MR. All treated patients experienced significant decreases in MR severity that were maintained throughout 6-month follow-up. The AltaValve offers a novel design with distinct features that limit procedural risk, mitigate complications, and potentially expand patient treatment.

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PERSPECTIVES

WHAT IS KNOWN? The AltaValve is a novel TMVR system that uses an atrial fixation anchoring mechanism.

WHAT IS NEW? The AltaValve TMVR system demonstrates safety and efficacy among 30 patients with symptomatic MR, with good valve function at 6 months.

WHAT IS NEXT? Longer follow-up and larger number of patients treated are needed to confirm the results of the AltaValve EFS.

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KEY WORDS mitral regurgitation, mitral valve, transcatheter mitral valve replacement

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