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Valve: New Technology

Early Feasibility Study with the SATURN Transapical Mitral Valve Replacement Device

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ABSTRACT

PURPOSE To report the outcomes of the early feasibility study of transapical transcatheter mitral valve replacement (TMVR) with the SATURN System (InnovHeart, Milano, Italy) to treat patients with severe functional mitral regurgitation.

DESCRIPTION Five high surgical risk patients underwent transapical transcatheter mitral valve replacement with the SATURN System at a single center. One-year follow-up is complete for all patients.

EVALUATION The valve was implanted successfully in all patients without any major adverse events. All patients were alive at the last follow-up. Kansas City Cardiomyopathy Questionnaire improved from a median of 63.5 (interquartile range, 19.6) at baseline to 99.0 (interquartile range, 21.6) at 1 year. Echocardiographic follow-up demonstrates stable valve function, no transvalvular or paravalvular mitral regurgitation, and absence of left ventricular outflow tract obstruction.

CONCLUSIONS At 1 year after transapical SATURN transcatheter mitral valve replacement, all patients are alive with quality of life improvement and favorable device hemodynamics. These initial results are promising and larger scale studies with continued follow-up are required to further elucidate the efficacy and safety of this novel technology.

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TECHNOLOGY

Surgical mitral valve (MV) repair is the preferred treatment option for patients with severe primary mitral regurgitation (MR). In patients with secondary MR, MV surgery is only recommended for patients undergoing open heart surgery for other indications, such as coronary bypass.[1] A substantial proportion of patients with MR are poor candidates for surgery due to their advanced age, medical comorbidities, or frailty. Mitral transcatheter edge to edge repair has demonstrated improvements in survival, heart failure symptoms, and hospitalization in patients with severe secondary MR and left ventricle (LV) dysfunction; however, a notable proportion of patients have residual MR, and persistent MR is associated with adverse outcomes.[2] Moreover, patients may not be suitable for transcatheter

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edge to edge repair due to leaflet length, calcification, mitral valve area, or other anatomical factors. Therefore, there is a growing effort to develop transcatheter mitral valve replacement (TMVR) devices for high surgical risk MR patients.[3] Current TMVR devices in clinical trial have a high anatomical screen failure rate due to mitral annulus size or concern regarding left ventricular outflow tract (LVOT) obstruction. The SATURN TMVR System (InnovHeart, Milano, Italy) utilizes a novel valve design that accommodates a wide range of mitral annular dimensions by reshaping and stabilizing the annulus. Furthermore, the valve has a low profile and restrains the anterior mitral leaflet, thus reducing the risk for LVOT obstruction. In this study, we sought to describe the early feasibility experience with transapical SATURN valve implantation.

TECHNIQUE

Ethics committee approval for the study was obtained at University Hospital Santaros Klinikos in Vilnius, Lithuania. All patients were determined to be high surgical risk by the local heart team. Between August 2020 and August 2022, 5 patients underwent transapical SATURN TMVR. Follow-up visits including clinical evaluation and transthoracic echo examination were scheduled at 30 days, 90 days, 6 months, 1 year, and 2 years post-implant.

DEVICE DESCRIPTION. The SATURN TMVR prosthesis has a multicomponent design consisting of an annular structure positioned around the native MV leaflets, a central valve, and a set of connecting arms to provide mechanical continuity between the central valve and the annular structure (Figure 1). The annular structure, split into lateral and medial annular segments, embraces the MV at the subannular level and reshapes and stabilizes the MV annulus. The central valve consists of a self-expanding nitinol stent supporting 3 prosthetic, bovine leaflets. The valve protrudes less than 13 mm into the LV and has no atrial flange. All patients were implanted with a 28-mm valve.

PREPROCEDURAL IMAGING AND SCREENING. All patients underwent both preprocedural cardiac computed tomography and transesophageal echocardiography to determine suitability for the SATURN device. Imaging was evaluated by the local heart team, an independent core laboratory, the study sponsor, and the Patient Screening Committee. Echocardiographic evidence using a multiparametric approach demonstrating at least moderate to severe (3+) MR was required. The mitral annulus size, subvalvular apparatus, and predicted neo-LVOT was assessed on cardiac computed tomography.

PROCEDURAL TECHNIQUE. After anesthesia induction, transapical access was obtained and a transapical port was placed. Next, the guidewire delivery system (GDS) was inserted through the apical port and its distal tip was positioned below the insertion of P2. A snaring basket embedded in a preshaped standard guiding catheter was externalized from the anterolateral lumen of the GDS and advanced atraumatically in the ascending aorta, crossing the aortic valve. Then, a standard J-tip guidewire was introduced into the LV through the posterolateral lumen of the GDS and advanced from P2 in the lateral aspect of the subannular groove towards the LVOT, embracing the mitral chordae. The guidewire was then snared in the ascending aorta to create the lateral loop. These steps were then repeated to create a medial loop. Once both loops were formed, the lateral and medial annular segments were advanced over their respective guidewire rails. The GDS was then removed and the valve delivery system (VDS) was introduced over the guidewire rails into the LV. Subsequently, the central valve was mechanically connected to the annular segments via the connecting arms, to create a single prosthetic unit. Finally, after positioning in a coaxial trajectory, the valve was unsheathed and deployed inside the annular structure, entrapping the native leaflets between the annular segments and the central valve (Figures 1, 2). After valve delivery, the apical access was closed. LV function and hemodynamics as well as the LVOT gradients were assessed by echocardiography. The post-implant antithrombotic strategy was aspirin in addition to either warfarin (target international normalized ratio, 2.5-3.5) or a non-vitamin K antagonist oral anticoagulant.

STATISTICAL ANALYSIS. Numerical data are presented as median and interquartile range (IQR), unless otherwise noted. The primary study endpoints were technical success, device success, and procedural success according to the Mitral Valve Academy Research Consortium definitions.[4]

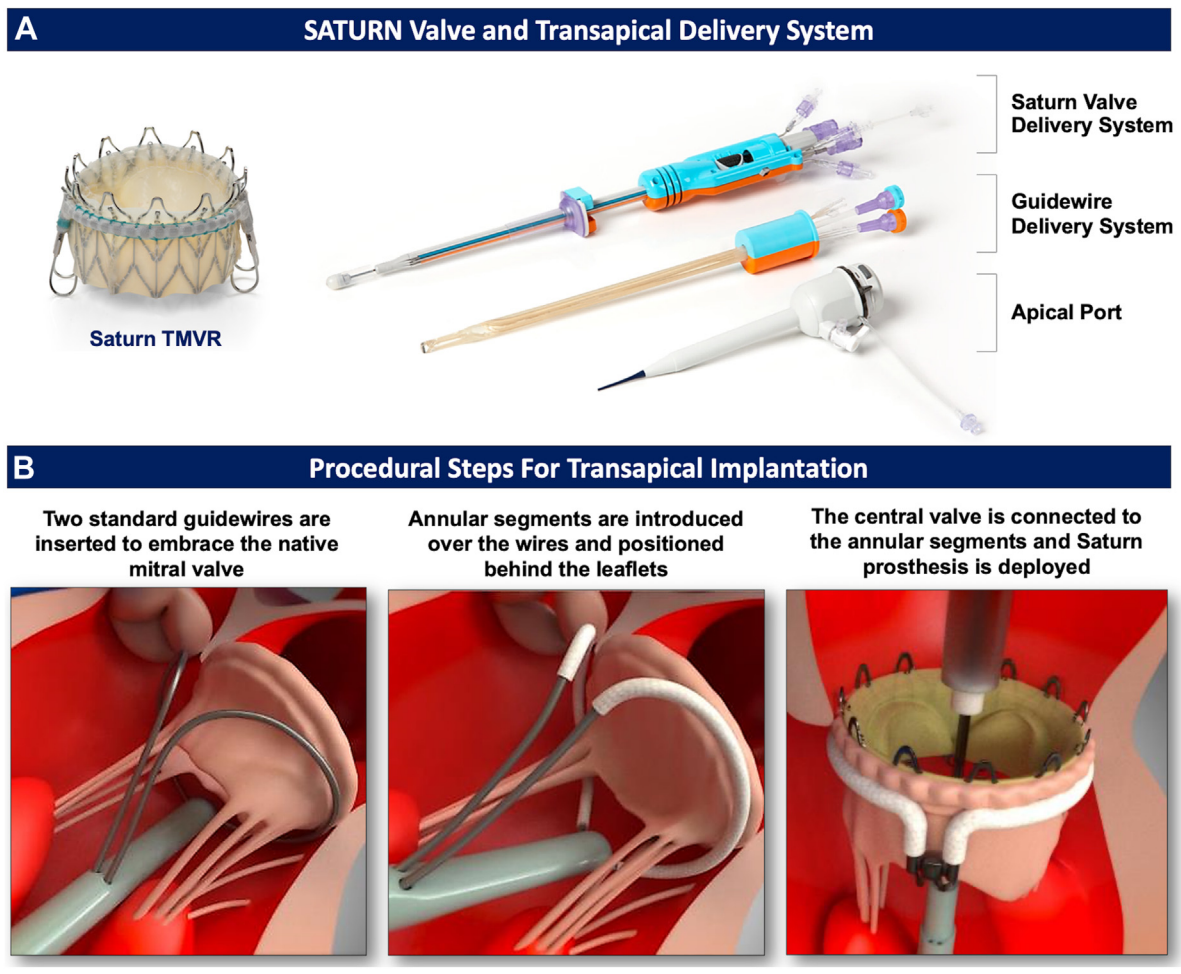

FIGURE 1 (A) SATURN (InnovHeart, Milano, Italy) transapical delivery system components. (B) Procedural steps (TMVR, transcatheter mitral valve replacement).

CLINICAL EXPERIENCE

BASELINE CHARACTERISTICS. The clinical and echocardiographic characteristics are presented in Table 1. All patients were male with a median age of 72 years (range, 63 to 76 years). The patients were at high surgical risk due to their comorbidities and functional status. The median left ventricular ejection fraction (LVEF) was 42.2% (range, 40 to 46%). MR severity was 3+ in three and 4+ in two of the patients.

CARDIAC COMPUTED TOMOGRAPHY EVALUATION. The median mitral annulus perimeter was 133 mm (range, 128-140 mm). The median anterior-posterior dimension was 36.0 mm (range, 33.5-41.5 mm) and intercommissural distance was 44.5 mm (range, 41.5-45.5 mm). None of the patients had severe mitral annular calcification. Anatomically, all patients had risk factors for LVOT obstruction including aortomitral angle $<110^{\circ}$, long anterior leaflet, or a sigmoidal septum. Nevertheless, the median predicted neo-LVOT was 601 mm^2 (range, 381-933 mm^2) in early systole and 464 mm^2 (range, 280-531 mm^2) in end systole.

PROCEDURAL RESULTS. All patients have completed 1-year post-procedure and 3 have completed the study with the 2-year follow-up. Technical success, device performance success, and procedural success were met for all patients. The median procedure time from apical port insertion to apical access closure was 77 minutes (range, 46-80 minutes) and dropped to 46 minutes in the last procedure. All patients were discharged home after a median length of hospital stay of 12 days (range, 7-13 days).

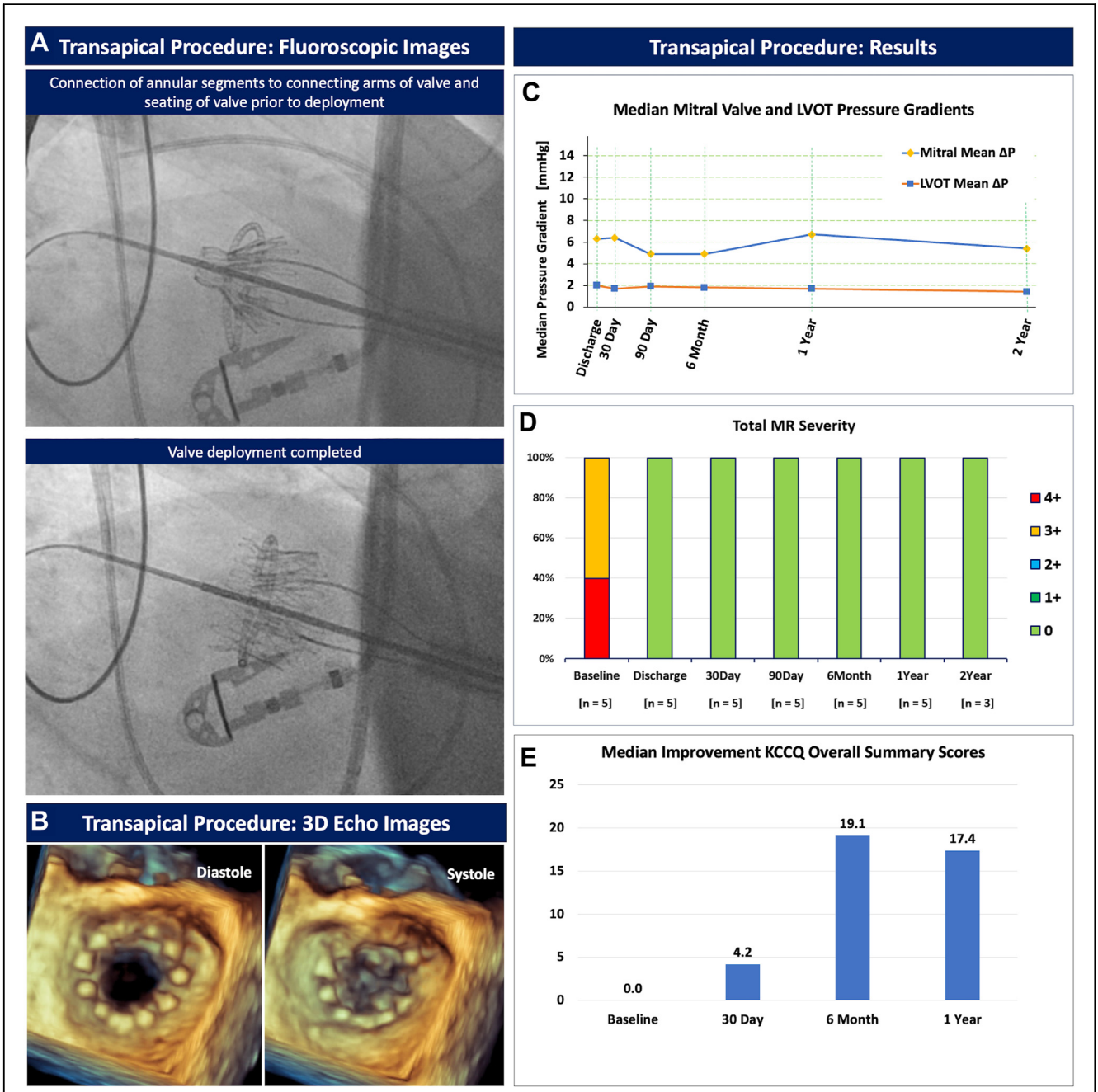

FIGURE 2 Representative (A) fluoroscopic and (B) 3-dimensional (3D) echo images of transapical SATURN (InnovHeart, Milano, Italy) valve implantation. (C) Longitudinal mitral valve and left ventricular outflow tract (LVOT) pressure gradients for the 3 patients who have completed the study. (D) Mitral regurgitation (MR) severity at baseline and follow-up timepoints. (E) Change in Kansas City Cardiomyopathy Questionnaire (KCCQ)-Overall Score from baseline to each of the follow-up timepoints.

No deaths, strokes, or any other Mitral Valve Academy Research Consortium-defined complications were observed during the hospitalization or 30-day follow-up period. At 30 days, echocardiography confirmed excellent valve position and function, proper sealing and anchoring, and no evidence of LVOT obstruction. The median mitral valve gradient was 5.6 mm Hg (IQR, 2.1 mm Hg) and the LVOT gradient was 1.7 mm Hg (IQR, 1 mm Hg). LVEF mildly decreased from a median of 42.2% (range, 40.0%-46.0%) at the time of screening to 34.1% at 30 days (range, 29.6%-45.3 %) but

TABLE 1 Baseline Patient Characteristics

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Demographics					
Age, y	72	76	75	63	65
Sex	M	M	M	M	M
Body mass index, kg/m^2	21.8	29.3	33.1	28.1	33.2
eGFR, mL/min/m^2	51	57	53	83	90
Previous cardiac surgery	Y	N	Y	N	N
Atrial fibrillation	Persistent	Paroxysmal	Permanent	None	Permanent
Pulmonary hypertension	Y	Y	N	Y	N
Diabetes mellitus	N	Y	Y	N	N
Myocardial infarction	Y	Y	Y	Y	N
New York Heart Association class	III	III	III	III	III
6-min walk test, m	350	465	275	420	390
STS-PROM, %	4.5	4.68	3.6	2.9	1.46
Kansas City Cardiomyopathy Questionnaire	82.6	96.9	50.5	63.0	63.5
Echocardiography					
LV end-diastolic diameter, cm	6.2	6.2	6.2	7.5	5.8
LV end-diastolic volume, mL	163.2	222	141.5	259	232
LV end-systolic diameter, cm	4.7	4.9	5.3	6.3	4.8
LV end-systolic volume, mL	88.1	130.8	84.9	147	127
LV ejection fraction, %	46	41	40	43	45
LV stroke volume, mL	64.8	84.4	52.6	68.4	47.7
MR grade	3+	4+	4+	3+	3+
MR EROA, cm^2	0.22	0.41	0.62	0.38	0.37
Regurgitant volume, mL	40.7	78	95	68.6	72.4
Tricuspid regurgitation grade	1+	1+	1+	0	N.E

eGFR, estimated glomerular filtration rate; EROA, estimated regurgitant orifice area; LV, left ventricle; MR, mitral regurgitation; N.E, not estimated; STS-PROM, The Society of Thoracic Surgeons Predicted Risk of Mortality score.

was stable thereafter. Cardiac output was maintained as the stroke volume increased by a median of 20.5% (range, 5.7%-38.2%) in the same time frame.

Echocardiographic parameters at follow-up are listed in Table 2. In the 3 patients who completed 2-year follow-up, the bioprosthetic mitral valve function remained stable with a median mitral valve gradient of 5.4 mm Hg (IQR, 1.7 mm Hg) and a median LVOT gradient of 1.4 mm Hg (IQR, 0.1 mm Hg). No paravalvular or intravalvular leak was observed after valve implantation.The longitudinal mitral valve and LVOT pressure gradients of the 3 patients who currently have completed the study are shown in Figure 2.

FUNCTIONAL OUTCOMES. All patients recovered well after TMVR and returned to independent living. At the last follow-up completed, all patients were alive with New York Heart Association functional class II. From baseline to 1-year follow-up, the Kansas City Cardiomyopathy Questionnaire-Overall Score increased by a median of 17.4 points (IQR, 24.7 points) from a median of 63.5 at baseline (IQR, 19.6 points) to 99.0 at 1 year (IQR, 21.6 points) (Figure 2).

TABLE 2 Echocardiographic Outcomes at 30 Days and 1 Year After Transapical SATURN TMVR

Outcome	30 Days (N = 5)		1 Year (N = 5)	
	Median	IQR	Median	IQR
LV end-diastolic diameter, cm	6.3	1.1	6.1	0.4
LV end-diastolic volume, mL	169.5	49.3	140.9	54.3
LV end-systolic diameter, cm	5.3	0.7	4.9	0.6
LV end-systolic volume, mL	104.1	50.0	88.3	36.7
LV ejection fraction, %	34.1	5.7	33.1	8.5
LV stroke volume, ml	69.5	16.5	80.2	28.8
LV outflow tract gradient, mm Hg	1.7	1.0	1.7	0.5
Mitral valve gradient, mm Hg	5.6	2.1	6.7	1.6
Mitral regurgitation grade	0	…	0	…
Paravalvular leak grade	0	…	0	…

SATURN transcatheter mitral valve replacement system, InnovHeart, Milano, Italy. IQR, interquartile range; LV, left ventricle; TMVR, transcatheter mitral valve replacement.

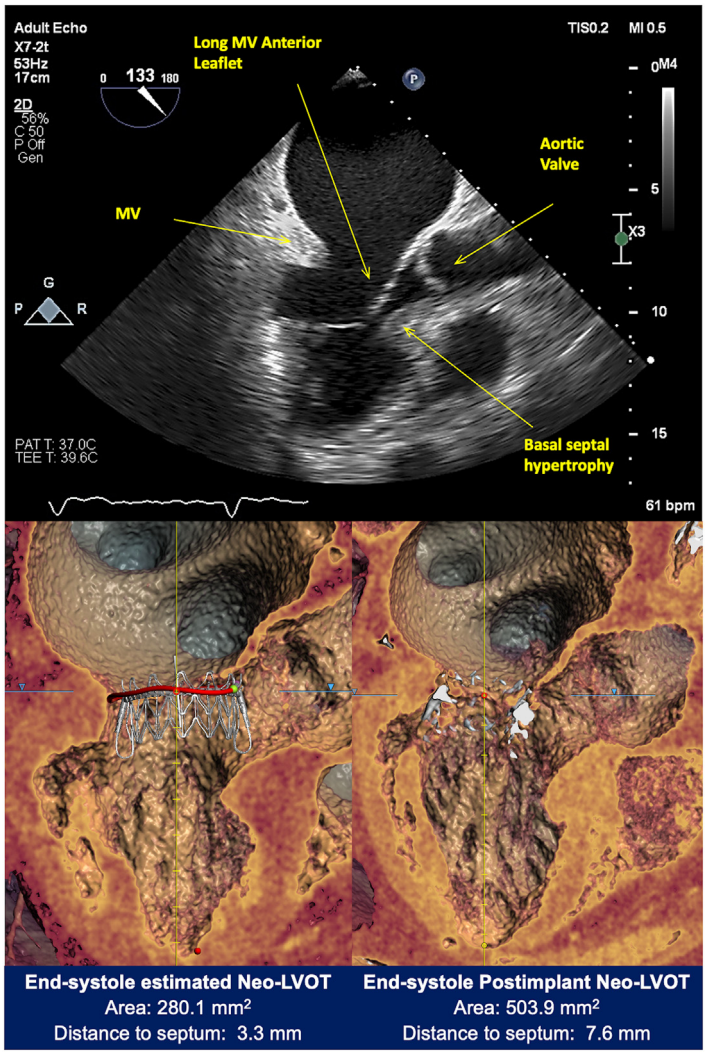

FIGURE 3 Example of high-risk left ventricular outflow tract (LVOT) obstruction patient treated with the SATURN valve (InnovHeart, Milano, Italy). (MV, mitral valve.)

COMMENT

This early feasibility experience demonstrates that the transapical implantation of the SATURN TMVR is safe and reproducible. Patients experienced stable valve function up to 2 years along with improved symptoms at follow-up. None of the patients had detectable LVOT gradients post TMVR despite their anatomic risk factors. We believe that the low profile of the valve without an outer frame, in combination with immobilization of the native anterior mitral leaflet, which prevents systolic anterior motion, results in favorable LVOT hemodynamics. This concept is supported by the widely patent LVOTs observed on post-TMVR computed tomography scans that were available (Figure 3).

Facilitated by the design of the prosthesis and the implant technique, which allows placement of the annular structure directly in the subannular space, the 28-mm valve size used in this study can accommodate a broad range of annulus sizes and can treat an intercommissural distance of up to 46 mm. The device reshapes mitral annulus similarly to a surgical annuloplasty. The remodeling at the base of the ventricle could contribute to better hemodynamic performance of the myocardial muscle (consistent increase in forward stroke volume after implant), but this hypothesis requires further clinical validation. In addition, a 31-mm valve size is now also available for intercommissural distances up to 53 mm. Importantly, the same 2 valve sizes can be implanted utilizing a transseptal delivery system for which preclinical testing has been completed.[5]

LIMITATIONS. The main limitation of this study is the small sample size with limited long-term follow-up. In addition, this early feasibility study was conducted at a single institution, therefore the findings cannot be generalized.

CONCLUSIONS. Our study demonstrates safe and effective transapical SATURN TMVR implantation with favorable valve performance. Clinical studies with a fully percutaneous, transseptal delivery system for implantation of the SATURN valve are anticipated in 2024.

FREEDOM OF INVESTIGATION

The tested technology was provided by InnovHeart. The authors had control of study design, methods used, outcome parameters, data analysis, and written report production.

DISCLAIMER

The Society of Thoracic Surgeons, The Southern Thoracic Surgical Association, and *The Annals of Thoracic Surgery Short Reports* neither endorse nor discourage the use of the new technology described in this article.

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DISCLOSURES

Kestutis Ručinskas reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel

reimbursement. Lauren S. Ranard reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Stefano Stella reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. David Hildick-Smith reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Matthew J. Price reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Vinayak Bapat reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Paolo Denti reports a relationship with InnovHeart that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement.

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