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Original Research

Lithotripsy-Assisted Transcatheter Mitral Valve Replacement for Severe Mitral Annular and Valve Calcification

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ABSTRACT

Background: Transcatheter mitral valve replacement (TMVR) is evolving; however, limitations include severe calcification of the mitral valve leaflets and mitral annular calcification (MAC), which may be associated with incomplete valve expansion. Shockwave intravascular lithotripsy (IVL)–assisted percutaneous mitral valvuloplasty to treat calcific mitral stenosis has been reported. We describe the first human use of IVL-assisted transseptal TMVR with the Intrepid valve to treat a severely calcified mitral valve in a patient with severe stenosis and regurgitation.

Methods: An 83-year-old man with rheumatic heart disease and severe MAC (MAC score, 10; calcium volume score, 7756 cm^3) presented with combined mitral stenosis and regurgitation (valve area, 1.5 cm^2; 3+ mitral regurgitation [MR]) and medically refractory heart failure symptoms and was enrolled into the APOLLO (Transcatheter Mitral Valve Replacement With the Medtronic Intrepid TMVR System in Patients With Severe Symptomatic Mitral Regurgitation) trial of Intrepid valve TMVR. Transseptal implantation of a 48-mm Intrepid valve was facilitated by Shockwave IVL delivered via two 8.0 × 60–mm M5+ balloons placed across the mitral annulus before implantation. Cerebral embolic protection during IVL and valve implant was provided by a Sentinel device and left subclavian balloon occlusion.

Results: Despite initial postimplant valve frame deformation and moderate central MR, postdilation achieved valve frame expansion and reduced MR. Echocardiography and computed tomography performed before hospital discharge and at 30 days show progressive valve frame expansion in the anteroposterior dimension, increased valve area, and resolution of MR.

Conclusions: Intravascular lithotripsy of severe MAC before self-expanding TMVR may enhance annular compliance, mitigate fibroelastic recoil, and minimize TMVR valve frame deformation. Although promising, further study is required before IVL is considered a routine adjunct for TMVR in severe MAC.

Introduction

Transcatheter mitral valve replacement (TMVR) has rapidly evolved. Although transapical TMVR devices have shown promise, procedure-related morbidity remains a concern. Transseptal TMVR appears feasible as reflected by reported off-label use of the Edwards SAPIEN balloon-expandable valve (BEV) in the mitral position.[1] Mitral annular calcification (MAC) is common in patients with mitral regurgitation (MR), ranging from 11.7%[2] to 42% in elderly patients.[3] Severe MAC and mitral valve leaflet calcification (MVC) pose challenges for surgical mitral valve repair/replacement.[4] Decalcifications with an ultrasound surgical aspirator and annular reconstruction are technically challenging. Operative risk is significantly increased in patients with severe MAC.[4,5]

In patients with high surgical risk, hybrid transatrial or transeptal deployment of the SAPIEN BEV in severe MAC has been reported.[6] Balloon predilation and postdilation of the native valve was performed in 26.7% and 53%, respectively, of patients undergoing transseptal TMVR, and overall device success was 53.3%.

Transseptal TMVR with self-expanding valves may be challenging in patients with severe MAC and MVC due to valve frame constraint and subsequent pin-wheeling of the valve leaflets with residual MR; however, transseptal BEV may provide better frame expansion at the risk of catastrophic annular disruption.

Lithotripsy-assisted balloon mitral valvuloplasty has been reported[7,8]; however, balloon dilation of severe MAC and MVC carries a risk of systemic embolism.

Abbreviations: IVL, intravascular lithotripsy; MAC, mitral annular calcification; MR, mitral regurgitation; MVC, mitral valve leaflet calcification; TMVR, transcatheter mitral valve replacement.

Keywords: lithotripsy; mitral annular calcification; transcatheter mitral valve replacement.

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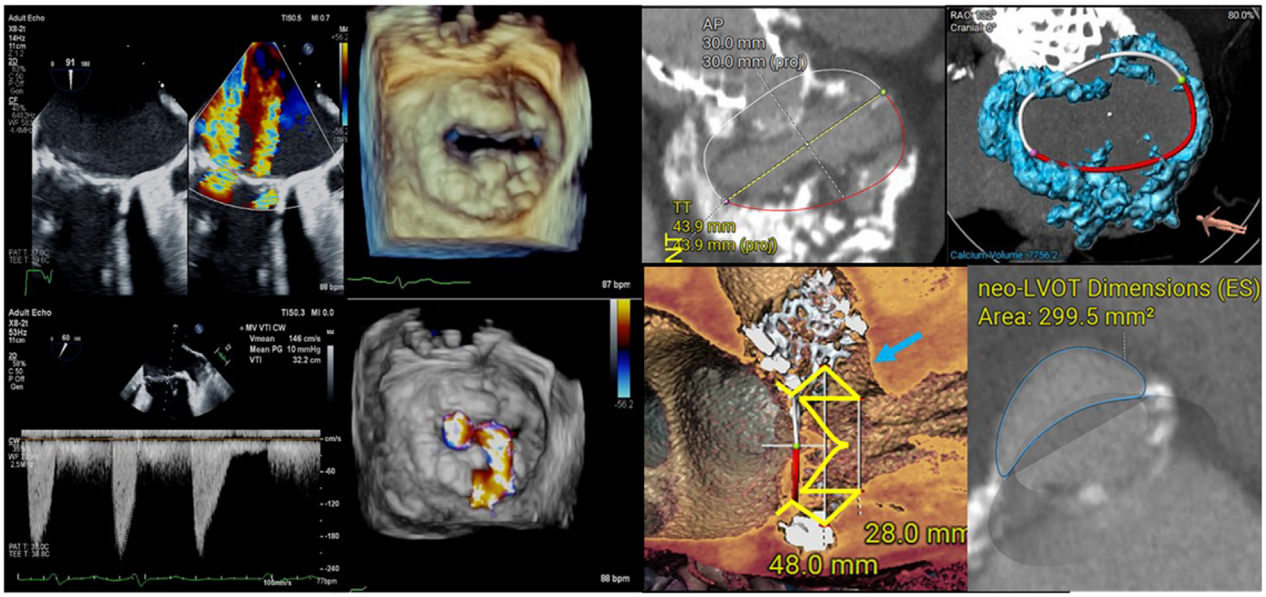


Figure 1.
Severely calcified mitral valve with grade 3+ regurgitation. Mean gradient of 10 mm Hg. Computed tomography analysis suggests a 48-mm Intrepid valve based on perimeter sizing. Calcium volume score was 7756 cm^3. Neo-left ventricular outflow tract (LVOT) was 300 mm^2 in early systole.

We describe the first human use of lithotripsy-assisted transeptal TMVR with the Intrepid valve (Medtronic) using cerebral embolic protection of all the great vessels in a patient with symptomatic severe mitral stenosis and MR due to severe MAC/MVC.

Methods

Case description

An 83-year-old man with rheumatic mitral and aortic valve disease, prior transcatheter aortic valve replacement for aortic stenosis (2018), and atrial fibrillation presented with worsening, medically refractory dyspnea and was noted to have severe mitral stenosis/MR.

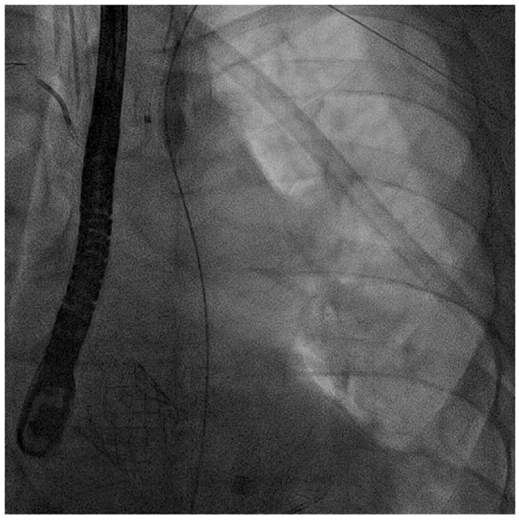


Figure 2.
Cerebral protection with SENTINEL filters in the right innominate and left common carotid with left subclavian balloon occlusion.

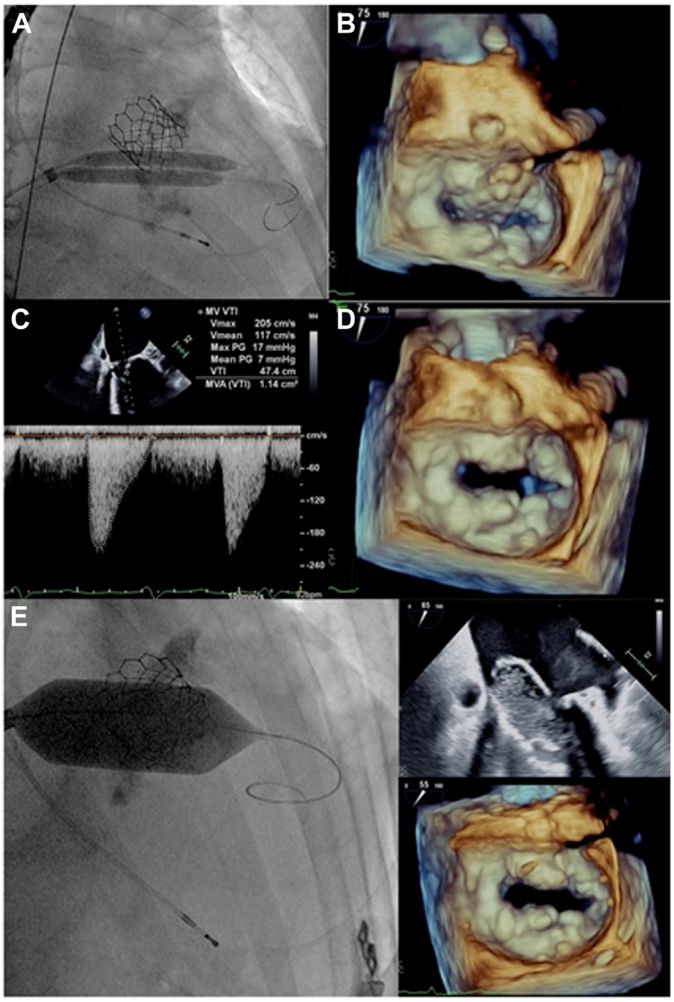
Baseline imaging

A transthoracic echocardiogram revealed normal left ventricular systolic function, a normal bioprosthetic aortic valve function (mean gradient, 11 mm Hg), and severe MAC/MVC. The mean mitral gradient was 10 mm Hg, the mitral valve area by continuity was 0.9 cm^2, and MR was grade 3. Transesophageal echocardiogram (TEE) revealed severely calcified leaflets, thickened chordae, and severe MAC (Figure 1). Mitral valve area was 1.5 cm^2, and grade 3+ MR (Carpentier type IIIA) with multiple jets was observed. Cardiac catheterization revealed right atrial pressure of 13 mm Hg, pulmonary systolic pressure of 50 mm Hg, pulmonary capillary wedge pressure of 30 mm Hg, cardiac index of 2.1, and minimal coronary disease.

Cardiac computed tomography angiography analysis in the APOLLO (Transcatheter Mitral Valve Replacement with the Medtronic Intrepid TMVR System in Patients With Severe Symptomatic Mitral Regurgitation) trial core laboratories revealed a MAC score of 10, a calcium volume score of 7756 cm^3, and dense MAC/MVC (Figure 1). The equipment was sized to a 48-mm Intrepid valve with oversizing of 20% in perimeter, 9% in commissural diameter, and 54% in anteroposterior (AP) diameter for the patient. The neo-left ventricular outflow tract at end-systole was 300 mm^2. The femoral vein, inferior vena cava, and left atrium were adequately sized to accommodate valve deployment.

Procedure details

Following signed informed consent for the APOLLO trial, the patient was approved for the MAC arm of the trial, and the procedure was performed in a hybrid operating room under general anesthesia with TEE guidance. To prevent systemic embolization, SENTINEL (Boston Scientific) cerebral embolic protection of the right innominate and left common carotid arteries was performed. Left vertebral artery protection was provided during valvuloplasty and TMVR by inflating a 10 × 40–mm Admiral balloon (Medtronic) in the ostium of the left subclavian artery (Figure 2). Right femoral vein access was obtained by surgical cut-down, and a 22F DrySeal Sheath (Gore) was inserted through which a transseptal Baylis TorFlex sheath (Boston Scientific) was advanced. A transseptal puncture was performed 4.5 cm above the mitral valve plane, a



Central Illustration.
(**A**) Two 8-mm Shockwave M5+ balloons across mitral valve annulus. (**B**) Transesophageal echocardiogram of Shockwave balloon inflation. (**C**) Mitral valve gradient decreased after Shockwave. (**D**) Increased mitral valve annulus and mobility of leaflets after 120 pulses of lithotripsy energy delivery. (**E**) A 26-mm True balloon inflation results in larger mitral valve area without increase in mitral regurgitation.

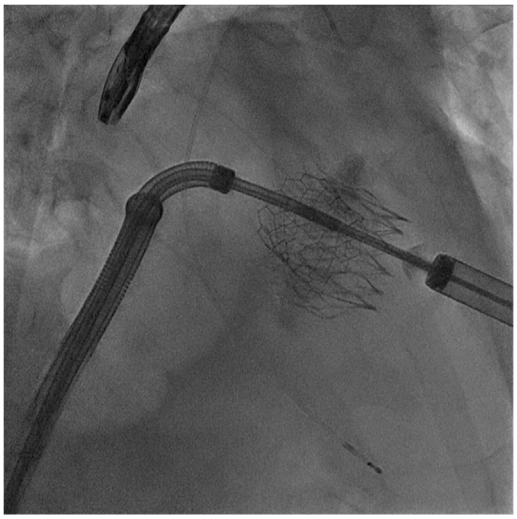


Figure 3.
A 48-mm Intrepid valve deployed during rapid pacing. A SAPIEN S3 valve is seen in the aortic position.

Safari wire (Boston Scientific Corporation) was advanced into the left atrium, and the intraatrial septum was dilated with a 14 × 40–mm Admiral balloon. A NAGARE tip-deflecting sheath (Terumo) was then advanced into the left atrium, and a pigtail catheter was advanced into the left ventricle (LV). The Safari wire was placed into the LV, and a 14F Mullins sheath (Cook) was advanced through which two 0.014-inch Grand Slam wires (Asahi) were placed into the LV. Two 8 × 60–mm Shockwave M5+ balloons were advanced across the mitral valve annulus with the middle emitters aligned with the annular plane, and lithotripsy was performed after inflating both balloons to 4 atm by delivering 4 rounds of 30 pulses each (total 120 pulses) with brief balloon deflation between pulse rounds (Central Illustration). The Safari wire was reinserted into the LV, and a 26-mm True balloon (Becton Dickinson) was placed across the mitral valve and inflated during rapid ventricular pacing until complete balloon expansion was achieved. The balloon, Mullins sheath, and Safari wire were removed and exchanged for a Lunderquist wire (Cook Medical), which was placed into the left upper pulmonary vein. Over this wire, the 37F TMVR sheath (Medtronic) was placed through which a 48-mm Intrepid valve was advanced into the LV. The valve was deployed using TEE guidance during rapid pacing (Figure 3). Postdeployment, moderate central MR and a valve gradient

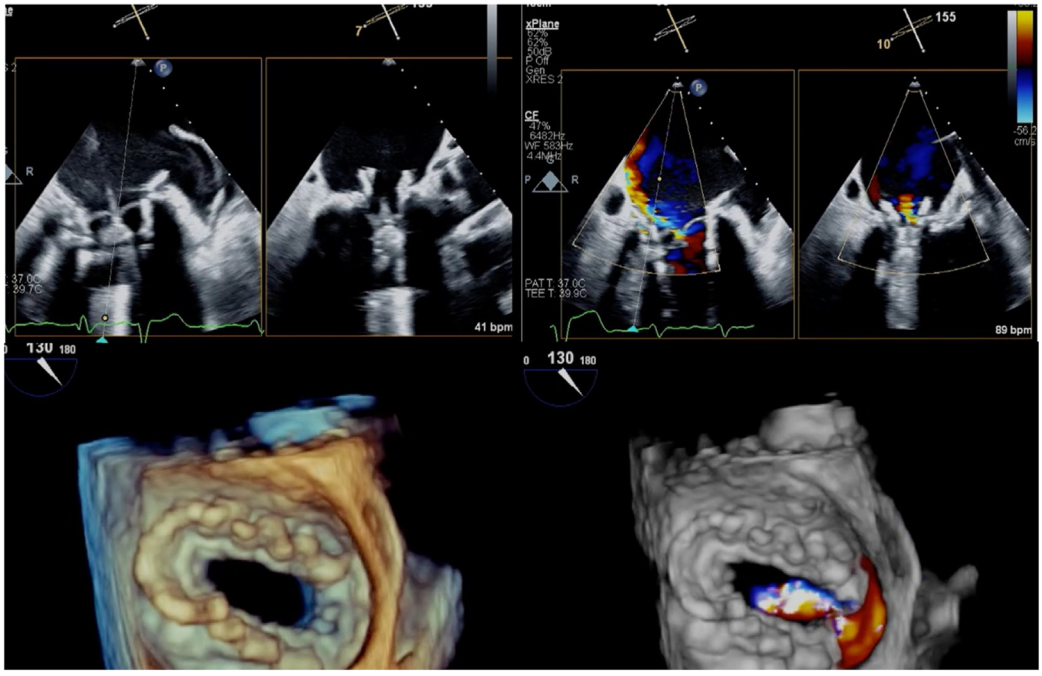


Figure 4.
Intrepid valve is constrained in the anteroposterior dimension. Valve leaflet misalignment causes eccentric mitral regurgitation.

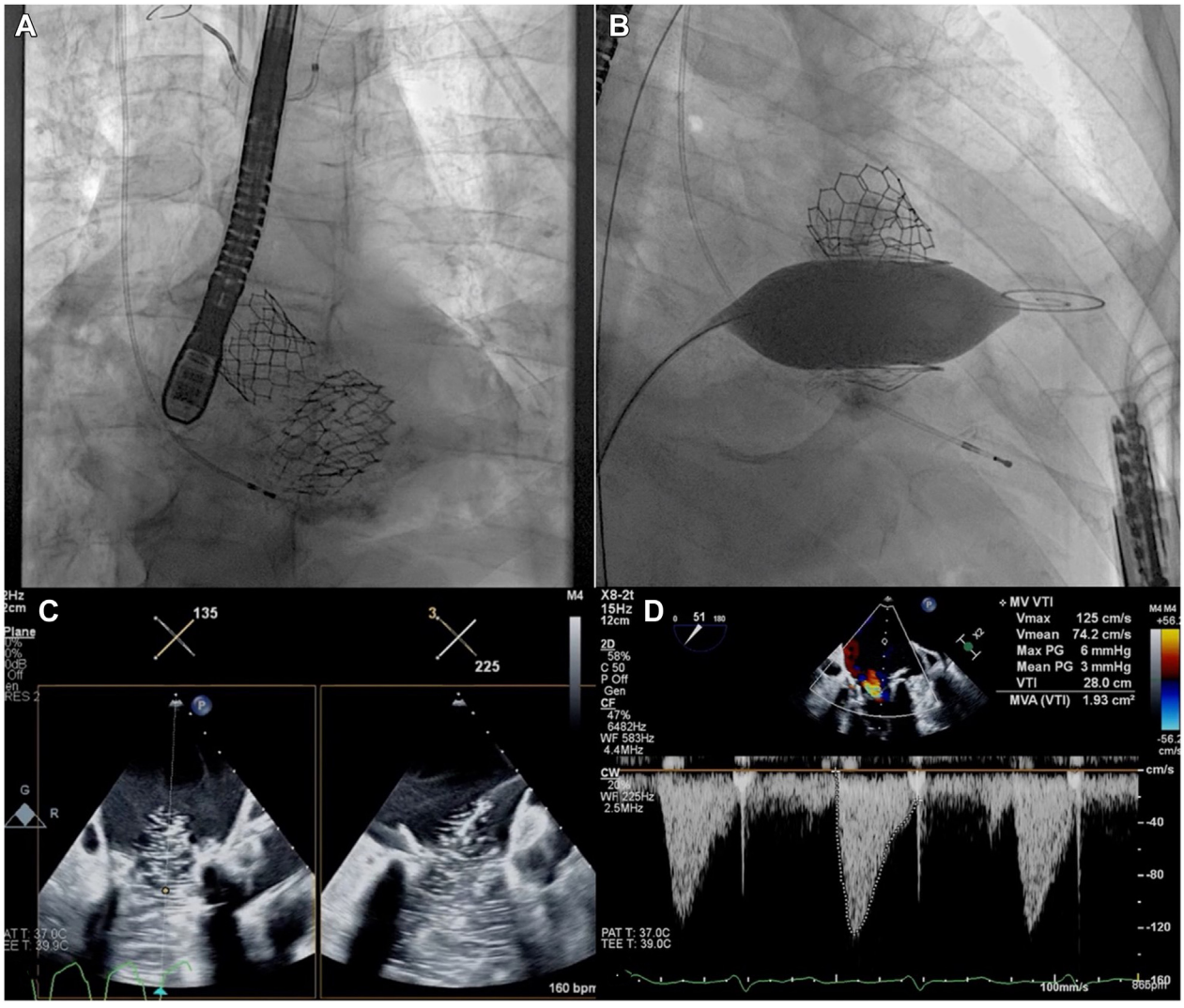


Figure 5.
(**A**) Fluoroscopy reveals constrained Intrepid valve frame. (**B**) Balloon postdilation with a 28-mm Z-MED balloon. (**C**) Expansion of the Z-MED balloon in anteroposterior and commissural dimensions. (**D**) Final mitral valve gradient of 3 mm Hg.

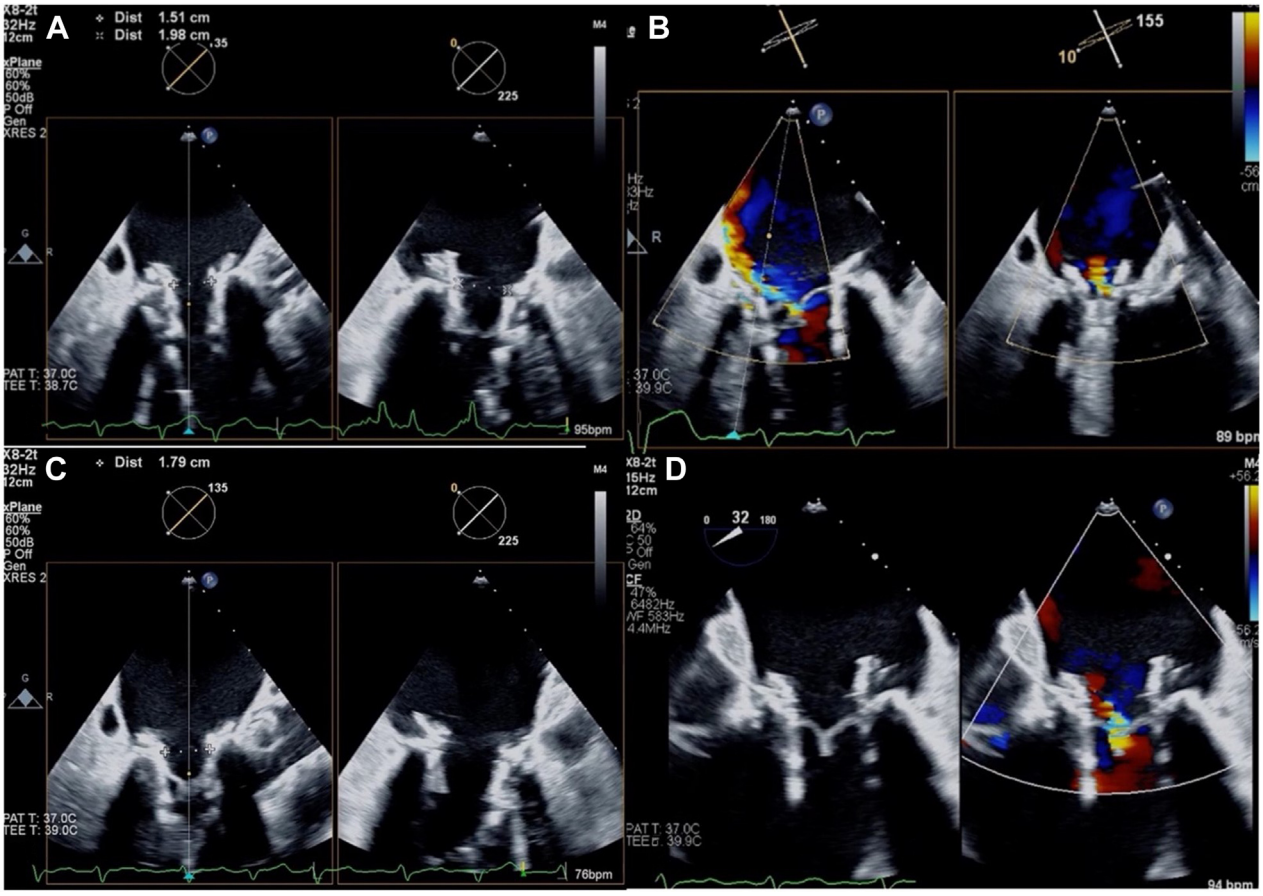


Figure 6.
(**A**) Valve frame dimension before postdilation constrained at 1.51 cm in the anteroposterior dimension. (**B**) Moderate eccentric mitral regurgitation before postdilation. (**C**) Anteroposterior valve dimension increased to 1.8 cm after postdilation. (**D**) Mild eccentric mitral regurgitation after postdilation.

of 4 mm Hg were observed. Moderate valve frame deformation was noted in the AP dimension (15.8 mm), with complete expansion in the lateral dimension by TEE and fluoroscopy (Figures 4 and 5). Postdilation was performed with a 28-mm Z-MED balloon (B. Braun) (Figure 5). Valve frame expansion (AP dimension, 19.5 mm) was observed fluoroscopically and on TEE with residual grade 2 central MR and a mean gradient of 4 mm Hg (Figure 6). This result was considered adequate, and the septal defect was not closed. The patient remained hemodynamically stable and was discharged on the third postoperative day.

Postprocedural imaging

Echocardiograms obtained before hospital discharge and at 30 days revealed mild (1+) mitral regurgitation, a mean gradient of 4 mm Hg, and progressive circularization of the valve frame. Predischarge and 30-day computed tomography angiography revealed progressive valve frame expansion in the AP dimension (21.9 mm and 22.4 mm, respectively) (Figures 7 and 8). In the AP dimension, the ventricular edge of the frame expanded from 23.2 mm to 24.6 mm and the inflow edge of the frame expanded from 19.5 mm to 21.8 mm.

Discussion

The surgical approach to MAC and MVC requires advanced surgical techniques and expertise. TMVR for native valve disease may be a reasonable alternative in patients with high surgical risk, yet MAC and MVC continue to be challenging for both self-expanding valves (Tendyne [Abbott], Intrepid) due to constraints during deployment as well as BEVs (SAPIEN S3 and M3), which risk injury and/or rupture of the mitral annulus.

Shockwave intravascular lithotripsy (IVL) of calcified mitral annulus and leaflets before TMVR may improve leaflet pliability, enhance annular compliance, mitigate fibroelastic recoil, and prevent valve frame deformation. The mechanism of action for coronary and peripheral vascular IVL appears to be multiplanar calcium fracture. As no transcatheter IVL device has been developed specifically for mitral valve application, we placed two 8-mm M5+ balloons side-by-side with the point of greatest sonic pressure wave impact (middle emitter) positioned at the level of the annulus. The IVL balloons were in contact with calcified valve leaflets and annulus but did not extend into the valve commissures. Despite the lack of intravascular imaging documentation, we believe that lithotripsy was effective in modifying MAC/MVC in this case, as reflected by an immediate increase (after IVL) in valve dimensions and progressive circularization/expansion of the valve over time following implantation. Although combined Sentinel and balloon occlusion of the left subclavian may provide effective global cerebral embolic protection, further studies are required. Although anecdotal, this case will hopefully prompt a larger-scale evaluation of IVL-facilitated TMVR in severe MAC/MVC and pan-cerebral embolic protection. Further clinical research is required before IVL can be a routine adjunct to TMVR.

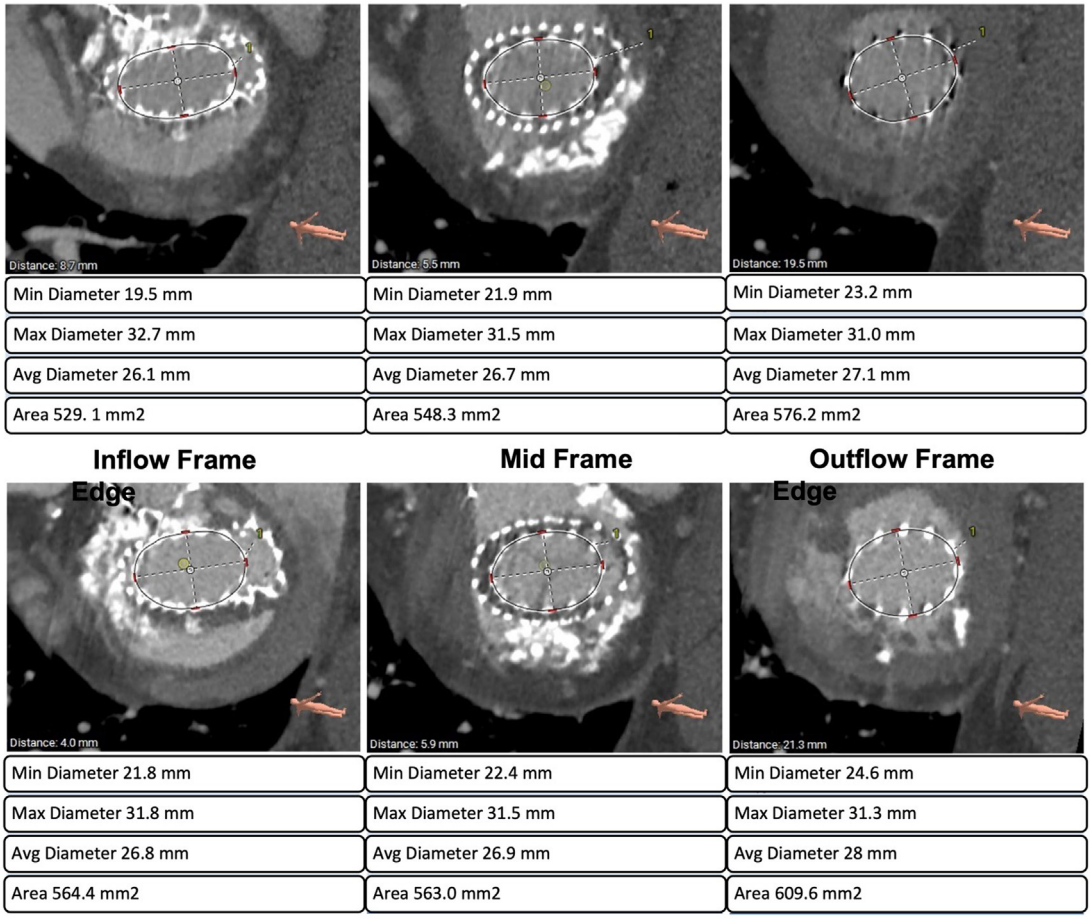


Figure 7.
Cardiac computed tomography angiography performed on postprocedural day 3 (top row) and day 30 (bottom row) revealed progressive circularization of the valve over time with the growth of the anteroposterior valve diameter to 21.8 mm from 19.5 mm and area to 564.4 mm^2 from 529.1 mm^2 (12% and 7% increase, respectively).

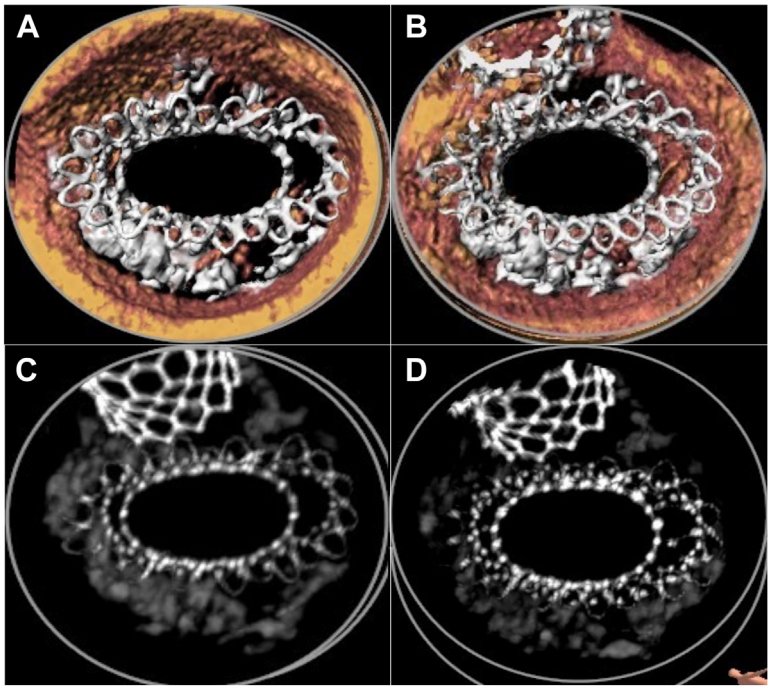


Figure 8.
Comparisons between computed tomography angiography performed on postprocedural day 3 and day 30 showed circularization of the valve. (**A**) 3-Dimensional color reconstruction at day 3. (**B**) 3-Dimensional color reconstruction at day 30. (**C**) Maximum intensity projection at day 3. (**D**) Maximum intensity projection at day 30.

Declaration of competing interest

Puvi Seshiah, Santiago Garcia, Joseph Choo, J. Michael Smith, Geoffrey A. Aswini, and Terri Steward are subinvestigators for the APOLLO trial, sponsored by Medtronic. Dean J. Kereiakes is a consultant for Shockwave Medical, Inc.

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Ethics statement and patient consent

This research was performed in accordance with ethical guidelines and following The Christ Hospital institutional review board approval. The patient signed informed consent for participation in the APOLLO trial.

Peer review statement

Given his role as Deputy Editor, Dean J. Kereiakes, had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Sandeep Nathan.

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