



Expert review

Transcatheter Aortic Valve Replacement for Aortic Regurgitation: A Case-Based Review



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Aortic regurgitation (AR) is the third most common valvular heart disease and its prevalence increases with age. Surgical aortic valve replacement remains the standard treatment but is often deferred due to perceived high surgical risk and frailty, leaving nearly one-third of patients with severe AR untreated. Transcatheter aortic valve replacement (TAVR) offers a less invasive alternative, but off-label use of transcatheter valves designed for aortic stenosis has been limited by anchoring difficulties, valve embolization, and residual regurgitation. Dedicated devices have addressed these challenges with tailored anchoring mechanisms and demonstrated improved procedural success. This case-based review explores the evolving role of TAVR for AR through 3 patient vignettes that highlight practical considerations for device selection, anchoring strategies, and complication management. While outcomes with dedicated systems are encouraging, further research should establish TAVR in AR treatment. In parallel, device iterations are required to curtail procedure-induced conduction disturbances and broaden anatomical eligibility.

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Aortic regurgitation (AR) is the third most common valvular heart disease and its prevalence is rising in aging populations.^{1,2} Any degree of AR is seen in 15% of the elderly population (>65 years), including moderate-to-severe AR in 1.6%.³ Chronic AR results in continued left ventricular (LV) volume overload, initially compensated by LV dilation and eccentric hypertrophy. Over time, these compensatory mechanisms fall short, resulting in more wall stress, progressive LV dysfunction, and ultimately heart failure. Patients with untreated severe AR have a 2-year mortality rate that exceeds 20%. Surgical aortic valve replacement is the gold standard for treatment; however, a third of patients with severe AR remain untreated.^{4–8} This undertreatment is caused by multiple factors. AR is characterized by a clinically silent disease progression and often reveals itself when patients are older and present with comorbidities and frailty.

Therefore, there is an unmet need for a less invasive alternative to surgery. Transcatheter aortic valve replacement (TAVR) revolutionized the treatment of severe aortic stenosis (AS) and is firmly established in clinical guidelines. However, the distinct pathology and anatomical differences of AR as compared to AS pose significant hurdles to TAVR implementation for AR.

In this review, we discuss the technical challenges and the current management strategies for AR with TAVR through 3 case vignettes, which highlight current limitations and future perspectives.

TAVR for Pure Native AR: The Journey From Off-Label to Dedicated Systems

Anatomical challenges cause anchoring issues

The primary challenge in treating pure native AR with TAVR stems from the anatomy. The aortic annulus is typically noncalcified, dilated, elliptical, and often accompanied by an enlarged ascending aorta and LVOT. Additionally, aortic regurgitation induces volume overload of the LV and is associated with larger-than-normal stroke volumes. These anatomical and pathophysiological factors have led to significant difficulties when using “off-label” transcatheter heart valves (THV) that were originally designed for AS and typically leverage the presence of calcium for anchoring.

Off-label experience

Early off-label experience with the self-expanding supra-annular CoreValve (Medtronic, Minneapolis, MN, USA) in pure AR established feasibility but exposed these anchoring limitations.^{9,10} In 1 multicenter registry of 43 patients, 32 (74%) patients experienced Valve Academic

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Research Consortium (VARC)-2 procedural success; 8 patients (19%) required a second valve implantation, and 9 patients (21%) ended up with moderate-to-severe residual AR.⁹ Outcomes did improve with experience and newer device iterations. In the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies (STS/ACC TVT) Registry analysis of 230 AR cases (81 CoreValve and 149 Evolut R), device success was higher with the Evolut (87% vs 72%), including lower rates of device migration (3% vs 10%), and moderate-to-severe residual AR at 30 days (6% vs 19%).¹¹ Although mortality decreased, it remained substantial with 10% 30-day mortality (compared to 19% in the CoreValve group).

The supra-annular ACURATE neo/neo2 (Boston Scientific, Marlborough, MA, USA) self-expanding valve consisted of stabilization arches and an external pericardial sealing skirt to enhance anchoring and limit paravalvular leak (PVL). It had a so-called top-down deployment and was also used off-label in AR. In 3 observational studies comprising 53 patients, device success ranged from 88% to 100%, with moderate-to-severe PVL reported in 0–8% of cases.^{12–14} Across these studies, 3 patients required a second valve and 1 patient died within 30 days. The ACURATE program was stopped after the ACURATE IDE trial demonstrated inferior clinical outcomes relative to the commercially available valves in the US.¹⁵

Balloon-expandable valve systems have also been utilized. Notably, in the French multicenter S3AR study ($n = 37$), where 15–25% oversizing was encouraged, the SAPIEN 3 (Edwards Lifesciences, Irvine, CA, USA) achieved 95% device success with no moderate-to-severe residual AR at 30 days.¹⁶ However, valve migration/embolization occurred in 4 patients (11%), 2 (5%) patients required a repeat procedure and 3 patients (8%) died within 30 days.

In an international Myval (Meril Life Sciences, Vapi, Gujarat, India) registry ($n = 113$), VARC-3 technical success was 95%, with 9% moderate-to-severe AR at discharge and 4% valve embolization rate.¹⁷ There was 5% mortality at thirty days. Myval offers the largest valve sizes, and the 32-mm Myval was utilized in 72% of cases.

Larger multicenter studies combining various off-label TAVR devices confirmed the limitations of off-label use of nondedicated devices. In a global registry by Yoon et al., including 331 patients, newer-generation valves improved device success (81% vs 61%), by reducing second-valve implantation (13% vs 24%) and moderate-to-severe residual AR (4% vs 19%).¹⁸ Similarly, the PANTHEON registry evaluated 201 patients with pure native AR treated with various nondedicated THVs and reported a device success rate of 76%, limited by a 15% rate of valve embolization and a 10% incidence of moderate-to-severe PVL. Thirty-day mortality rates exceeded 10%.^{18,19} Outcomes did not differ between self-expanding and balloon-expandable platforms.

Current guidelines have expressed caution regarding the use of TAVR with off-label devices in high-surgical-risk patients with pure AR.^{4,5} Dedicated TAVR systems were primarily developed to address the anchoring challenge.

Trilogy

The Trilogy (JenaValve Technology, Irvine, CA, USA) is a self-expanding nitinol THV with porcine-pericardial leaflets. It features 3 radiopaque locator clips that grasp the native cusps, for anchoring with commissural alignment. It is available in 23-mm (Small), 25-mm (Medium), and 27-mm (Large) sizes, suitable for annular perimeters ranging from 66 to 90 mm. Originally designed for transapical delivery, the Trilogy has transformed into an 18 Fr transfemoral system, and transaxillary and transcaval access have also been described.^{20–24}

In the multicenter transapical JenaValve CE-mark study, 67 high-risk patients (mean logistic EuroSCORE 28%) underwent transapical implantation of the JenaValve system.²⁵ Procedural success was achieved in 60 patients (90%), with conversion to surgery in 4 (6%)

and valve-in-valve implantation in 2 (3%). At 30 days, all-cause mortality occurred in 5 patients (8%) and new permanent pacemaker implantation in 8 (12%).

In the pivotal ALIGN-AR trial 500 high-surgical-risk patients with symptomatic native AR (180 premarket approval and 320 continued-access patients) were treated with the transfemoral JenaValve Trilogy which demonstrated high device success at 96% and a low valve embolization rate of 2%.^{26,27} At 30 days, the rates of moderate-to-severe residual AR were 2%, permanent pacemaker implantation 23% and 30-day mortality 1%. One-year survival reached 92%.²⁷

Some key anatomical exclusion criteria for the JenaValve Trilogy included bicuspid valve morphology, straight ascending-aorta length <55 mm, and annular angulation >70°. Global commercial availability has been limited so far despite the Conformité Européenne (CE) mark since 2021. In the United States, Trilogy is only available in the continued access program following the ALIGN-AR trial, pending FDA approval.

J-valve

J-Valve (JC Medical Inc., Burlingame, CA, USA) is a self-expanding Nitinol THV with bovine-pericardial leaflets and 3 U-shaped anchor rings that grasp the native leaflets. The device is available in 5 sizes (22 to 34 mm), covering annular perimeters from 57 up to 104 mm. It is delivered via an 18 Fr steerable transfemoral system and alternative access routes like transcarotid, transaxillary, and transcaval have also been employed.²⁸

In the transfemoral early feasibility study (25 patients) procedural success was achieved in 92% (23/25), with no device embolizations or migrations, 2 (10%) pacemaker implantations and no cardiovascular deaths at 30 days.^{29,30} In a North-American compassionate-use registry (27 patients), overall procedural success was 81%, and 100% in the last 15 cases after device and protocol refinement.²⁸ At 30 days, there was 1 death (4%), 1 nonfatal stroke, 3 new pacemakers (13%), and no moderate-to-severe residual AR.²⁸

Although bicuspid morphology is not a formal contraindication for the J-Valve and has been used compassionately, experience remains limited and notably, the U.S. Early Feasibility Study excluded bicuspid patients.^{28,29} The J-Valve is currently only available in study setting. Long-term durability and hemodynamic performance of the transfemoral J-Valve system remains unclear.³¹

Hanchor valve

The Hanchor valve (Healing Medical Technology, Shanghai, China) is the first balloon-expandable THV designed for AR, with porcine leaflets and a nitinol anchoring element that grasps the leaflet.³² The delivery system is designed for transfemoral access. The multicenter HAVE-AR trial in China ($n = 128$).³² reported a procedural success rate of 96%, with a 2% valve embolization rate and no instances of moderate or severe paravalvular leak at 30-day follow-up. Bicuspid aortic valves and horizontal aortas were allowed.

Improved anchoring and clinical outcomes of dedicated TAVR systems

A recent meta-analysis by Samimi et al. involving 2,162 patients who underwent TAVR for pure AR, demonstrated that dedicated systems (JenaValve Trilogy and J-Valve) achieved higher device success rates (93% vs 82%) and lower valve embolization (2% vs 8%), moderate-to-severe residual AR incidence (2% vs 5%), and 30-day mortality (3% vs 9%) compared to off-label systems.³³ Dedicated systems also reduced the need for reinterventions (4% vs 10%) and permanent pacemaker implantations (11% vs 20%) at 30 days. At 1 year, all-cause mortality was substantially lower in patients treated with dedicated devices (6% vs 24%). These findings strongly support the use of dedicated TAVR devices as safer and more effective alternatives for high-risk patients with pure native AR.

Conduction disturbances and pacemaker implantation

Permanent pacemaker implantation remains a frequent complication after TAVR for pure AR, even with dedicated devices. The Trilogy system has consistently shown 30-day PPM rates of 23–24%, as reported in the ALIGN-AR trial, the PURPOSE registry, and a multicenter European Trilogy registry.^{22,26,34}

Reported PPM rates for other dedicated devices appear lower: 10% (2/20) in the J-Valve early feasibility study and 13% (3/24) in the compassionate-use series for the J-Valve and 12% (15/125) in the Hanchor HAVE-AR cohort. However, these comparisons should be interpreted with caution given the small sample sizes and potential differences in patient selection. It is also important to note that pure AR is associated with higher PPM rates after SAVR.^{35,36}

Baseline conduction abnormalities and larger aortic root and annular dimensions have emerged as the most consistent predictors of pacemaker need post-TAVR for pure AR with dedicated devices.^{22,26,34} By contrast, valve oversizing, which is a well-established predictor of conduction injury in aortic stenosis, predicted PPM only in the PURPOSE registry, which included nondedicated devices, but not in ALIGN-AR or the European Trilogy registry. These findings suggest that the mechanisms of conduction injury in AR-TAVR may differ from those in calcific stenosis, potentially involving larger LVOT dimensions imposing more stress on the conduction system at baseline, absence of protective calcification around the conduction system, and arguably procedural factors such as implantation depth and oversizing. Further research is needed to refine device design and procedural strategies to reduce PPM.

Case-Based Discussions and Integrated Topics

Case 1: JenaValve trilogy and reverse cardiac remodeling

An 81-year-old frail woman described NYHA class II and was referred for TAVR for severe aortic regurgitation. Baseline echocardiography showed an LVEF of 34%, moderate mitral regurgitation and a markedly dilated LV with LV indexed end-diastolic volume (LVEDVi) of 160 mL/m² and LV indexed end-systolic volume (LVESVi) of 103 mL/m². Multidetector computed tomography demonstrated an

annular perimeter of 74 mm with minimal calcification (Agatston score: 302 AU), a dilated ascending aorta (50 mm), and suitable iliofemoral access for transfemoral delivery. After discussion in the multidisciplinary heart team, the patient was considered at increased surgical risk, with a Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score of 4.0%, advanced age, frailty and LV dysfunction and was scheduled for transfemoral TAVR with an S-size Trilogy valve. The procedure was performed without complications, and postprocedural echocardiography confirmed optimal valve positioning with a mean gradient of 5 mmHg and no paravalvular or central regurgitation. At follow-up, the patient reported improved exercise tolerance (NYHA Class I). At 18-month follow-up, she remained in NYHA class I, with marked reverse remodeling: LVEDVi crimped to 73 mL/m², LVESVi to 37 mL/m², LVEF improved to 55%, LV mass decreased by 36% (217 g to 139 g), and only trace mitral regurgitation remained (Figure 1). Aortic dimensions were stable. This case underscores the role of TAVR for pure AR in frail, elderly patients at high surgical risk and its potential to catalyze LV reverse remodeling.

Reverse remodeling

Reverse remodeling after TAVR for pure AR has been reported across several studies using dedicated TAVR platforms. In the HAVE-AR trial, LVEDD decreased significantly from 59 mm to 48 mm at 30 days after implantation of the Hanchor valve, with a concomitant rise in LVEF.³² The J-Valve early feasibility study showed similar early reductions in LV dimensions (LVEDD from 59mm to 52mm) in combination with LVEF improvement.²⁹ The ALIGN-AR trial confirmed reverse remodeling through 1 year, with LVEDVi decreasing from 82 mL/m² to 63 mL/m² and a reduction in mean LV mass from 173 g/m² to 118g/m².^{26,27} These findings parallel the findings of reverse remodeling after surgical aortic valve replacement or repair of chronic AR.^{37,38}

Case 2

A 65-year old woman with a prior medical history of VVI-pacemaker and HeartMate III left ventricular assist device (LVAD), which had been implanted 1 year earlier as destination therapy for dilated cardiomyopathy, presented with NYHA III symptoms and a moderate-to-severe AR

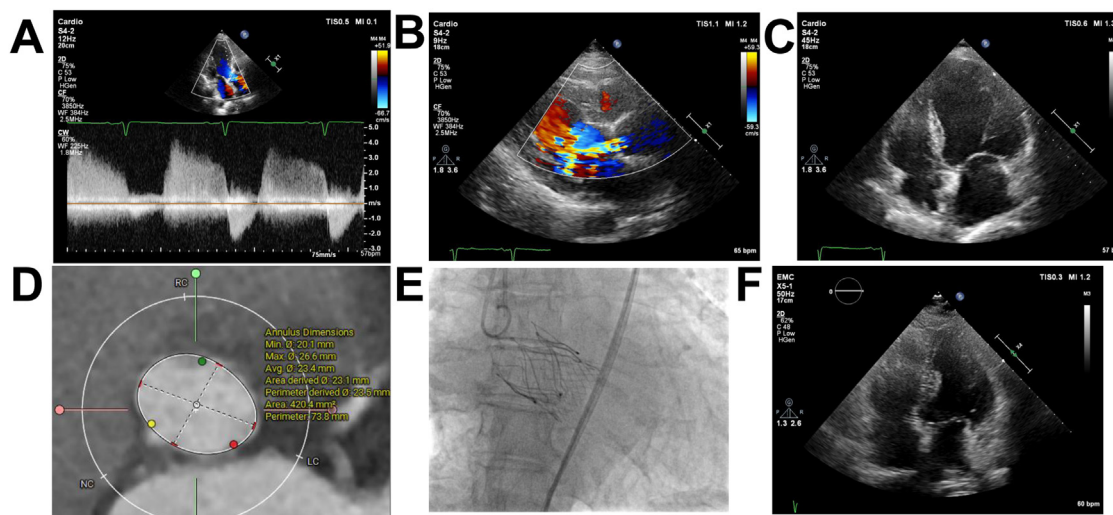


Figure 1. Echocardiographic and CT-imaging before and after TAVR with JenaValve Trilogy in pure aortic regurgitation. (A–C) Preprocedural transthoracic echocardiography (TTE) demonstrating severe aortic regurgitation and left ventricular dilatation (LVEDD 55 mm, LVEF 34%, LVEDVi 160 mL/m², LVESVi 103 mL/m²). (D) Multidetector computed tomography (CT) showing an annular perimeter of 74 mm with minimal calcification (Agatston score: 302 AU). (E) Intra-procedural fluoroscopy during transfemoral implantation of an S-size JenaValve Trilogy prosthesis. (F) Follow-up TTE at 18 months demonstrating an improved systolic function (LVEF 55%), and reverse remodeling (LVEDD 53 mm, LVEDVi 73 mL/m², LVESVi 37 mL/m²).

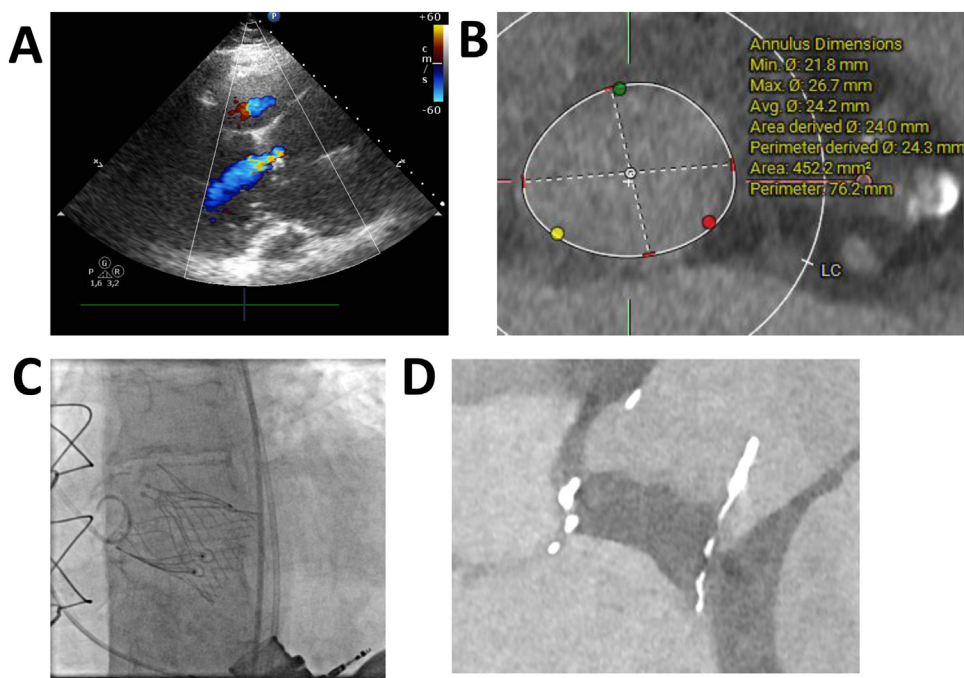


Figure 2. Multimodality Imaging of Severe Aortic Regurgitation Treated with JenaValve Trilogly in LVAD patient. (A) Color Doppler echocardiography showing continuous aortic regurgitation pre-TAVR, (B) Preprocedural CT demonstrating an aortic annulus perimeter of 76.2 mm, (C) Postprocedural angiogram with a 25 mm JenaValve Trilogly in situ, (D) Postprocedural CT showing leaflet thrombus with reduced leaflet motion.

on echocardiography. The AR worsened at higher LVAD speeds. preprocedural computed tomography (CT) assessment revealed an annulus area of 452 mm², a perimeter of 76 mm, LVOT area of 466 mm², and an ascending aorta diameter of 46 mm, as shown in Figure 2. Iliofemoral vessels were suitable for transfemoral TAVR with a 25-mm JenaValve Trilogly. Her STS-PROM was 3.6% and in the context of prior LVAD implantation, the heart team deemed her at prohibitive risk for surgical aortic valve replacement and recommended transfemoral TAVR. She underwent an uneventful transfemoral TAVR under local anesthesia. postprocedural echocardiography and CT confirmed successful implantation without residual AR. However, a leaflet thrombus with reduced leaflet motion was identified on follow-up CT imaging, prompting the initiation of aspirin on top of her vitamin K antagonist therapy. The patient was subsequently discharged to a cardiac rehabilitation program. Two months later she experienced a TIA and after 4 months she improved to NYHA II. This case illustrates the role of TAVR in LVAD patients with concomitant AR.

TAVR for patients with LVAD and AR

In LVAD patients, AR may develop due to the mechanical stress exerted on the aortic valve and ascending aorta, which may accelerate valvular deterioration and progressive aortic dilatation.³⁹ Early continuous-flow devices were associated with moderate-to-severe AR in up to 30% of patients within 1 year. Contemporary cohorts with the HeartMate III, reported moderate-to-severe AR in 8% of patients at 1 year of follow up.⁴⁰

During TAVR procedures in LVAD patients, temporary reduction of LVAD speed is mandatory to decrease transvalvular gradients and suction forces, thereby mitigating the risk of valve migration. However, the resulting low-flow state postprocedure can increase the risk of transcatheter heart valve (THV) thrombosis, as observed in our case. Leaflet thrombosis, characterized by hypo-attenuated leaflet thickening and reduced leaflet motion, has been reported in up to 32% of TAVR procedures.⁴¹ This complication may elevate transvalvular gradients,

predispose patients to embolic events, and accelerate structural valve deterioration. Uptitration of oral anticoagulation is generally advised.

Current literature on TAVR in LVAD patients is limited to small case series. Procedural success with dedicated devices appears encouraging.^{41,42} The JenaValve ALIGN-AR LVAD Registry (JENA-VAD; NCT06594705) is an ongoing prospective Registry on this topic.

Case 3

A 76-year-old man with a recent diagnosis of stage III nonsmall cell lung cancer, for which chemotherapy was initiated, was diagnosed with severe AR and depressed LV function following an acute heart failure event. Chemotherapy treatment was interrupted until aortic valve intervention was performed and the patient was deemed too frail for surgery, despite STS-PROM of 1.7%.

Computed Tomography revealed an annulus area of 683 mm² and perimeter of 93 mm with limited valvular calcification (Agatston 149 AU). The annulus exceeded the maximum perimeter for JenaValve Trilogly (which is the only dedicated system available at our center). Iliofemoral vessels were suitable for transfemoral TAVR. Given the patient's frailty and need to swiftly restart chemotherapy, there was heart team consensus for TAVR with a balloon expandable Myval Octacor 32-mm (Meril Life Sciences, Vapi, India). This corresponded with an 18% annular oversizing. TAVR was performed under local anesthesia and with rapid pacing at 220bpm. The Myval embolized into the aorta immediately following deployment. The embolized Myval was successfully snared and secured above the aortic annulus. A 34-mm Evolut XL valve was implanted within the Myval for valve fixation and resulted in favorable hemodynamics, and trivial paravalvular leakage (Figure 3E). postprocedurally, the patient developed complete heart block requiring temporary pacemaker support. The conduction issue resolved and he was subsequently discharged home on day 4 and remained well at 1-month follow-up, with no elevated gradient across the tav-in-tav construction.

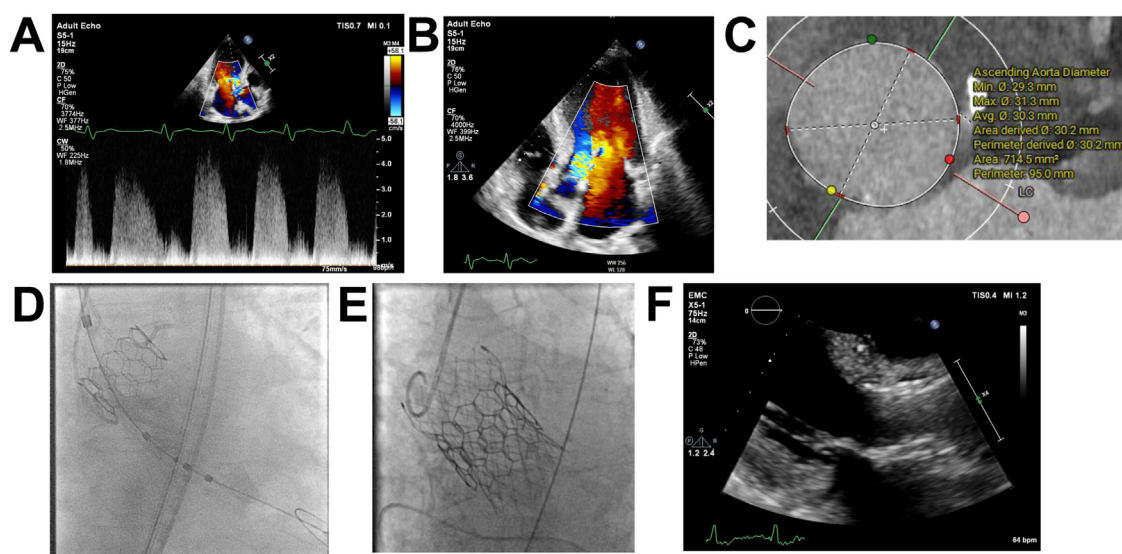


Figure 3. Multimodality imaging of aortic regurgitation treated with TAV-in-TAV following embolization of a Myval Octacore 32 mm. (A–B) Preprocedural transthoracic echocardiography demonstrating moderate left ventricular function and moderate-to-severe aortic regurgitation, (C) Preprocedural CT showing a large, noncalcified annulus (perimeter: 93 mm; Agatston score: 149 AU), (D) Fluoroscopy revealing embolized 32-mm Myval Octacore valve, (E–F) Angiographic and echocardiographic confirmation of successful valve-in-valve implantation with a 34-mm Evolut XL deployed within the embolized Myval.

Procedural techniques to prevent and manage valvular embolization with nondedicated systems

Incremental oversizing is advised for anchoring nondedicated valve platforms in noncalcified native aortic valves with severe AR. However, excessive oversizing (>20%) carries the rare but fatal risk of annular rupture and may paradoxically increase the risk of valve embolization, particularly for self-expanding valves.^{19,43} The latter is hypothesized to occur due to distal migration of the flared and oversized frame towards the LV.⁴³

Deployment with rapid pacing is advised to reduce stroke volume and better stabilize the device during deployment. Postdilatation may be hazardous and promote valve migration in the absence of calcium and was an independent predictor of THV embolization in the Multicenter Pantheon registry.¹⁹ A TAV-in-TAV may be the best solution for suboptimal valve positioning or migration of a nondedicated valve and should be preferred over postdilatation.

Percutaneous retrieval (snaring) and conversion to surgery may be alternative strategies in selected cases.

Future Perspectives

Current follow-up data with dedicated transcatheter systems remains relatively short. Two-year outcome data have been reported for the Trilogy valve, and 5- to 8-year data are available for a small early transapical cohort treated with the J-Valve.^{27,31,44} Longer-term surveillance is needed to determine structural valve deterioration in the high-stroke-volume setting of pure aortic regurgitation, especially if transcatheter therapy is extended to younger or lower-risk patients.

The ARTIST trial (NCT05289020) is a randomized controlled trial comparing the JenaValve Trilogy with SAVR in low- and intermediate-risk. Beyond comparative trials, continued innovation in device design and implantation techniques is vital. Such advancements aim to reduce postprocedural complications, like AV-conduction disturbances, and broaden anatomical eligibility, include patients with larger annular dimensions and bicuspid aortic phenotypes.

The Cusper device (Cuspa, Nazareth, Israel) represents a novel transcatheter valve repair concept, aiming to reduce AR. It comprises a small nitinol clip (3.4 × 16 mm) with a 6 mm pericardial sac, delivered via a 16 Fr percutaneous system.⁴⁵ It attaches to a single aortic cusp to mitigate the regurgitant jet. In a porcine proof-of-concept study, the device reduced moderate-to-severe AR to trivial levels. While promising, it remains in early preclinical development with no human experience to date.

Conclusion

Dedicated TAVR systems is reshaping the treatment landscape for high-risk patients with pure AR by addressing long-standing challenges of device anchoring in noncalcified aortic valves. Early clinical and hemodynamic data are encouraging. Ongoing research is needed to define long-term durability and, mitigate acquired conduction disorders. Randomized controlled trials evaluate the role for these dedicated systems in patients with pure AR at lower operative risk.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Rutger-Jan Nuis reports a relationship with Vitor Pharma that includes: funding grants. Rutger-Jan Nuis reports a relationship with Meril Life Sciences Private Limited that includes: funding grants. Rutger-Jan Nuis reports a relationship with Edwards Lifesciences Corporation that includes: consulting or advisory. Rutger-Jan Nuis reports a relationship with Abbott Vascular Inc that includes: consulting or advisory. Rutger-Jan Nuis reports a relationship with Boston Scientific Corporation that includes: consulting or advisory. Joost Daemen reports a relationship with ACIST Medical Systems Inc that includes: funding grants and speaking and lecture fees. Joost Daemen reports a relationship with Abbott Laboratories Inc that includes: funding grants and speaking and lecture fees. Joost Daemen reports a relationship with Boston Scientific Corporation that includes: funding grants and speaking and lecture fees. Joost Daemen reports a relationship with MicroPort Scientific Corporation that includes: funding grants. Joost Daemen reports a relationship with PIE that includes: funding grants and speaking and lecture fees. Joost Daemen reports a

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CRedit authorship contribution statement

Lucas Uchoa de Assis: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Andrea Mariani:** Writing – review & editing, Writing – original draft, Methodology. **Antigone Kostea:** Writing – review & editing, Writing – original draft, Methodology. **Rutger-Jan Nuis:** Writing – review & editing, Writing – original draft, Methodology. **Joost Daemen:** Writing – review & editing, Writing – original draft, Methodology. **Nicolas M. Van Mieghem:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Conceptualization.

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