

Transcatheter Interventions for Pure AR: From Off-Label Use to Dedicated Devices

Challenges of TAVR in the treatment of pure aortic regurgitation and how dedicated devices can overcome them.

By Sara Waezsada, MD, and Tanja K. Rudolph, MD

Surgical aortic valve replacement (SAVR) is the standard therapy for patients with severe aortic regurgitation (AR) according to current guidelines. Despite increased mortality, only one in four patients with severe AR receives surgical therapy.¹ To date, transcatheter treatment options for patients with increased operative risk and advanced age have been limited. Although transcatheter aortic valve replacement (TAVR) is the recommended intervention in the majority of elderly patients with aortic stenosis (AS), several technical factors limit its use in the treatment of AR. The off-label use of commercial transcatheter heart valves (THVs) in AR has been associated with a higher risk of malpositioning, migration, and significant residual regurgitation, mainly due to the absence of valve calcification leading to insufficient anchoring.² However, the development of dedicated THVs has recently shown the potential to overcome these technical challenges, as initial studies demonstrate promising technical and functional results.³⁻⁷

OFF-LABEL DEVICES AND TECHNICAL CHALLENGES

TAVR in AS was first described in 2002 and has emerged as standard of care for a considerable proportion of patients with AS; however, the first case that showed its feasibility in pure AR was reported in 2010.⁸ In 2013, the first multicenter registry evaluating off-label use of a self-expanding THV (CoreValve, Medtronic) for TAVR in pure AR confirmed general feasibility with a procedural success rate of 74.4%, but it also highlighted technical limitations, as a second valve had to be implanted in 18.6% of cases.⁹ These limitations were persistently observed in subsequent reports of off-label

AR treatment with several self-expanding and balloon-expandable devices, emphasizing an inferior efficacy profile compared to TAVR in AS. The main challenge associated with the use of first-generation THVs in the setting of AR is the occurrence of transcatheter valve embolization and migration (TVEM) due to the absence of valve calcification as an anchoring mechanism, dilated aortic dimensions, and a suction effect caused by the regurgitant jet.

In PURPOSE, a retrospective multicenter registry comparing the performance of off-label devices and dedicated devices for AR, the incidence of TVEM amounted to 15% in the collective treated with off-label devices.¹⁰ In the PANTHEON registry, the negative impact of TVEM on technical performance in AR was accompanied by higher mortality rates and an increased incidence of heart failure rehospitalization.¹¹ These findings illustrate why TAVR with an off-label THV remains problematic in patients with AR and why purpose-built devices that address these limitations are needed.

FIRST EXPERIENCE WITH DEDICATED DEVICES FOR AR

JenaValve

The self-expanding JenaValve Trilogy THV (JenaValve Technology, Inc.) is a second-generation device first approved in Europe in 2011, with CE Mark approval for the treatment of AR received in 2021. Although FDA approval of the device is currently pending, it is expected in 2025 based on the results of the ALIGN-AR study published last year. It was initially designed to avoid complications of TAVR in AS, such as paravalvular leak, conduction disturbances requiring pacemaker implantation, and stroke.¹²

The potential for JenaValve as dedicated device for the treatment of AR was first described in a case series in 2013 that documented promising technical and functional outcome.¹³ The specific design of the JenaValve differs from first-generation THVs in its ability to allow stable anchoring even in the absence of valve calcification. The device consists of a porcine pericardial valve attached to a nitinol frame. Three positioning feelers initially placed into the sinuses of the native valve enable an active clip fixation to the native leaflets after release of the prosthesis. Thus, the device does not require extensive radial force on the aortic annulus for stable positioning. The three available sizes of the device (23, 25, and 27 mm) cover annulus diameters from 21 to 27 mm. Although the first generation of the JenaValve system was designed for transapical delivery, it was withdrawn from the market in 2016 after the introduction of the next-generation transfemoral system. Both systems showed excellent technical success (96.7% and 95%) and sustained performance at 1-year follow-up in pivotal trials, including 30 patients treated with the transapical system and 180 patients treated with the transfemoral system. However, mortality was lower in the collective treated with the transfemoral system (8% vs 20% at 1 year).^{3,14} A real-world multicenter registry including 58 patients with pure AR validated these promising results.⁴

Despite superior procedural outcome of the JenaValve compared to off-label devices mostly due to a lower incidence of TVEM and residual AR, a high rate of permanent pacemaker implantation (PPI) of up to 24% as reported in the ALIGN-AR study should be noted.³ Although the rate dropped from 29% to 14% during the course of the trial, PPI rates remain high compared to those in TAVR for AS. In addition, the PURPOSE study comparing off-label and dedicated devices in TAVR for AR showed that PPI rates did not differ in both device groups, highlighting that this observation seems to be a general issue in the AR collective.¹⁰

J-Valve

Similar to the design of the JenaValve, the J-Valve (JC Medical) consists of a porcine aortic valve attached to a nitinol stent and three encircling U-shaped graspers that allow stable anchoring in the absence of valve calcification, analogous to the positioning feelers of the JenaValve. The first-in-human implantation of the device for AR was performed through transapical delivery in 2014 and demonstrated a high effectiveness of the system.⁵ A multicenter registry including 43 patients with severe AR confirmed high procedural success (97.7%) in the absence of severe adverse events. A low PPI rate of 4.7% was reported.⁶

Although the initial transapical J-Valve was available in four sizes (21-27 mm), the subsequently developed transfemoral system was designed to cover more dilated aortic dimensions, with sizes up to 34 mm, enabling implantation in annulus perimeters up to 104 mm. This characteristic of the J-Valve marks a crucial advantage compared to the JenaValve system, which can only be implanted in patients with a maximal annulus perimeter of 90 mm.

In the only real-world registry to date evaluating the performance of the transfemoral J-Valve, technical success was reported in 81% of the 27 included patients.⁷ Despite procedural success and inferior survival compared to the JenaValve, the results of the registry attest that interventional treatment of AR with the J-Valve is a safe and effective alternative for patients with increased surgical risk. In addition, a lower PPI rate was reported with the J-Valve transfemoral system compared to the JenaValve transfemoral system (13% vs 24%).^{3,7} Following these promising results, a pivotal trial is currently being conducted that will further assess the safety and efficacy of the J-Valve transfemoral system. The device has earned breakthrough device designation from the FDA, but so far has not reached the European market.

FUTURE PERSPECTIVES

Compared to the extensive evidence on TAVR in AS, data on its implementation in the treatment of AR remain limited. Nevertheless, a growing number of studies point to its feasibility and potential to become a valid alternative for patients with AR and increased operative risk. Dedicated devices have been shown to be superior to off-label devices in terms of technical results and outcome and should therefore be the focus of future studies, especially regarding long-term outcomes. Furthermore, investigational effort needs to be directed to a better understanding of underlying mechanisms responsible for the high incidence of postprocedural PPI. While current research is solely restricted to establishing TAVR as an alternative for inoperable patients, it remains unclear if noninferiority of TAVR to SAVR in AR is conceivable for certain patient collectives apart from high-risk patients in the future. ARTIST, the first randomized trial comparing TAVR with the JenaValve system to SAVR in patients with AR and at low to intermediate surgical risk (NCT06608823), has recently started recruitment and will be the first step to answer these questions. Although the significance of interventional treatment in AR needs to be further investigated, its potential to improve the long-neglected undertreatment of AR already is indisputable. ■

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