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REVIEW

Transcatheter Aortic Valve Replacement for Aortic Regurgitation – A Review

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Abstract

Transcatheter aortic valve replacement (TAVR) is currently a widely used option for patients with severe symptomatic aortic stenosis with high to low surgical risk. However, aortic regurgitation (AR) remains an "off-label" indication for TAVR, particularly for patients with mild or absent leaflet calcification or aortic annulus dimensions beyond the size of the bioprosthesis, which increase the risk of dislocation. With advances in transcatheter heart valve devices, the safety and efficacy of TAVR in treating patients with severe pure native AR has gained acceptance. This review examines current evidence and clinical practice, and presents technological advancements in devices for AR.

Keywords: transcatheter aortic valve implantation; transcatheter aortic valve replacement; aortic regurgitation; new generation devices

Abbreviations and Acronyms: TAVR, transcatheter aortic valve replacement; AR, aortic regurgitation; PNAR, pure native aortic regurgitation; LV, left ventricular; LVEF, left ventricular ejection fraction; SAVR, surgical aortic valve replacement; PVL, paravalvular leak; NGDs, new-generation devices; EGDs, early-generation devices; THV, transcatheter heart valve; PPA, post-procedural AR; STS, Society of Thoracic Surgeons Score; NYHA, New York Heart Association; PPI, permanent pacemaker implantation; MR, mitral regurgitation; STJ, sinotubular junction.

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Introduction

Aortic regurgitation (AR) affects approximately 13% of patients with isolated native left-sided valvular heart disease and occurs in up to 2% of all over 70 years of age [1]. Severe pure native aortic regurgitation (PNAR) is distinguished by the eccentric myocardial hypertrophy and volume overloading associated with structural modifications of the left ventricular (LV) cavity and progressive LV dysfunction. LV remodeling occurs as a result of cardiomyocyte enlargement stimulated by growth factors associated with the Frank–Starling mechanism. When compensatory ability is no longer present, the function of the left ventricle becomes permanently impaired and cannot be restored [2, 3]. Surgical aortic valve replacement (SAVR) is currently recommended for patients with chronic severe AR. However, a considerable proportion of

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patients tend to seek treatment in very late stages of disease progression, when the operative risk is prohibitive. Research has demonstrated that only 20% of patients diagnosed with severe AR and left ventricular ejection fraction (LVEF) between 30% and 50% opt for SAVR, whereas only 5% of those with LVEF levels below 30% receive valve replacement [1–4]. Patients who choose conservative treatment face a high risk of mortality (20% annual mortality rate). Therefore, less invasive treatment options for these patients must urgently be explored.

Since the first case of transcatheter aortic valve replacement (TAVR) in patients with severe aortic stenosis was successfully performed in 2002, the procedure had been performed more than 800,000 times in more than 65 countries as of 2021, including the entire spectrum of patient surgical risk [5–11]. Given the efficacy and safety of TAVR, researchers began to investigate treating patients with PNAR percutaneously. Data on early generation devices (EGDs) for TAVR in patients with PNAR have been published. However, owing to the absence of valve calcification and challenges in anchoring the bioprosthesis, the risks of valve embolization, malpositioning, and paravalvular regurgitation are exacerbated after percutaneous intervention. Technological changes have improved the performance of devices with retrievability, repositioning, and anchoring mechanisms. New-generation devices and dedicated devices for AR continue to emerge, and have been endorsed by the Food and Drug Administration or clinical trials. This article reviews the current evidence supporting TAVR for PNAR, and discusses current technological developments and future directions.

Devices and Clinical Evidence Supporting TAVR for PNAR

The first-in-human reports on the feasibility and safety of transcatheter heart valves (THVs) in treating AR used a non-dedicated device called the SAPIEN valve. This device was used in 2012 by D'Antoni et al. to treat a case of PNAR, with a left ventricle assistant device implanted, over the long term [12]. Subsequently, Roy et al. retrospectively analyzed a case series of 43 patients with PNAR at high surgical risk (mean age 75.3 ± 8.8 years, mean Society of Thoracic Surgeons Score (STS) 10.2 ± 5.3%), who received the first-generation CoreValve. The success rate was 97.7%, and 18.6% of patients required a second valve because of residual AR during the procedure. At 30 days, the rate of all-cause mortality was 9.3%, the rate of stroke was 4.7%, and the mortality at 1 year was 21.4% [13]. The summarized studies of TAVR for AR are presented in Table 1.

With the development of the valve device, several studies on patients with PNAR who received TAVR have been reported since 2017. Yoon et al. [20] have reported a cohort study of 331 patients with severe AR, 36% receiving EGDs and 64% receiving NGDs. The age of the included patients was 74.4 ± 12.2 years, and the STS score was 6.7 ± 6.7%. Compared with EGDs, NGDs showed a significantly higher rate of device success (24.4% vs. 12.7%), lower rate of second THV (12.7% vs. 24.4%), and lower rate of moderate to severe PPA (4.2% vs. 18.8%).

Significantly fewer comorbidities with the procedure were observed with NGDs, but no significant difference in 1-year all-cause mortality was found between devices (28.8% vs. 20.6%; $P = 0.13$). Of note, NGDs were associated with a significantly lower 1-year cardiovascular mortality (9.6%) than EGDs (23.6%) [20].

Yousef et al. have systematically reviewed the results of 175 patients with PNAR who underwent TAVR. The THVs included Direct Flow, Acurate TA, CoreValve, SAPIEN, JenaValve, J-Valve, and Lotus. Device success was achieved in 86.3% of patients, as defined by Valve Academic Research Consortium-2 (VARC-2) criteria [31], and no procedural deaths, annular ruptures, or myocardial infarction were observed. In a 30-day follow-up, the rates of mortality, second THV implantation, permanent pacemaker implantation (PPI), and moderate or severe paravalvular leak (PVL) were 9.6%, 11.3%, 10.7%, and 17.7%, respectively. Patients who received NGDs rather than EGDs had significantly better outcomes in terms of the rate of device success: (96.2% vs. 78.4%), residual AR (0.0% vs. 8.3%), and second THV implantation (1.7% vs. 23.4%) [32].

De Backer et al. have conducted a study on 254 patients with PNAR who underwent TAVR with high surgical risk, at 46 centers. The mean patient

Table 1 TAVR for PNAR: Characteristics of the Included Studies.

Author (year)	Country	Study design	No. of patients	Age (year)	Male sex	STS score	Logistic Euroscore	Reason surgery declined	Valve type	VARC criteria reported	Approach (reported)	Follow-up
Roy et al. (2013) [13]	Worldwide/ multicenter	Retrospective and prospective	42	75.3±8.8	20	10.2±5.3	NR	High risk	CoreValve	Yes	Femoral, subclavian, aortic, and carotid	12 months
Seiffert et al. (2013) [14]	Germany	Retrospective	5	66.6±7	4	NR	NR	Inoperable	JenaValve	Yes	Apical	3 months
Seiffert et al. (2014) [15]	Germany/ multicenter	Retrospective	31	73.8±9.1	20	5.4±3.6	23.6±14.5	Inoperable	JenaValve	Yes	Apical	6 months
Testa et al. (2014) [16]	Italy/multicenter	Prospective	26	73±10	16	13.1±2	24±8	Inoperable	CoreValve	Yes	NR	12 months
Wendt et al. (2014) [17]	Germany	Retrospective	8	72.5±8.4	5	7.9±3.4	34.0±7.9	High risk	Acurate TA	Yes	Apical	12 months
Schofer et al. (2015) [18]	Europe/multicenter	Retrospective	11	74.7±12.9	4	8.84±8.90	19.9±7.1	High risk	Direct Flow	Yes	Femoral	30 days
Wei et al. (2015) [19]	China	Prospective	5	74.8±8.9	3	NR	29.59	High risk	J-Valve	No	Apical	6 months
Yoon et al. (2017) [20]	USA/Europe/Asia/ multicenter	Retrospective and prospective	331	74.4 ±12.2	159	6.7±6.7	NR	Inoperable	CoreValve. Evolut R, Portico, Acurate, SAPIEN XT/SAPIEN 3, JenaValve, Lotus, Direct Flow, and J-Valve	Yes	Femoral, apical subclavian, aortic, and carotid	12 months
Sawaya et al. (2017) [21]	Germany/ multicenter	Retrospective and prospective	78	74±10	46	6.7±4.8	20.4±11.8	Inoperable	CoreValve, Evolut R, SAPIEN XT / SAPIEN 3, Lotus, and Direct Flow	Yes	Femoral and apical	30 days
De Backer et al. (2018) [22]	Europe/multicenter	Retrospective	254	74 ± 12	134	6.6 ± 6.2	NR	High risk	JenaValve, Engager, CoreValve EvolutR, Portico, Acurate, Lotus, Direct Flow, and SAPIEN XT/ SAPIEN 3	Yes	Femoral and apical	12 months
Liu et al. (2018) [23]	China/multicenter	Prospective	43	73.9±5.7	30	NR	25.5±5.3	High risk	J-Valve	Yes	Apical	1 year
Anwaruddin et al. (2019) [24]	USA/multicenter	Retrospective	230	68.7± 15.1	134	8.6±9.1	NR	NR	CoreValve and Evolut R	Yes	Femoral and apical	12 months
Li et al. (2020) [25]	China/Single center	Prospective	4	76.0± 6.9	3	NR	31.7±3.6	High risk	J-Valve	Yes	Apical	4 years
Gogia et al. (2020) [26]	USA/Single center	Prospective	11	77.6	NR	NR	NR	High risk	Jena Valve	NR	Femoral	6 months
Vahl et al. (2021) [27]	USA/multicenter	Prospective	71	74	NR	NR	NR	High risk	Jena Valve	Yes	Femoral	30-days
Yin et al. (2022) [28]	China/two centers	Retrospective	25	72.0±17.2	18	8±4.5	NR	Intermediate to high risk	CoreValve, Evolut R, J-valve, and SAPIEN XT	Yes	Femoral and apical	35 months
Schneeberger et al. (2022) [29]	Germany/single center	Retrospective	9	74.4±7.1	8	6.2 ± 3	NR	High risk	Acurate neo and neo-2	Yes	Femoral	30 days
Koch et al. (2023) [30]	USA/single center	Retrospective	34	68.8±12.2	25	3.96	NR	High risk	CoreValve, Evolut R, and Evolut Pro	Yes	Femoral and caval	30 days

age was 74 ± 12 years, and the mean STS score was 6.6 ± 6.2%. The patients underwent THV with either EGDs (43%) or NGDs (57%). On the basis of outcome assessment with VARC-2 criteria, NGDs had a significantly higher device success rate than EGDs (82% vs. 47%). In addition, NGDs had significantly lower rates of device misplacement (9% vs. 33%) and PPA (moderate or greater) (4% vs. 31%) than EGDs. Furthermore, NGDs showed significantly higher clinical effectiveness than EGDs at 30 days (72% vs. 56%). For both devices, undersizing and oversizing were correlated with a significantly elevated risk of device malpositioning [22].

Anwaruddin et al. have recruited 230 patients with primary severe native AR at high surgical risk who received the CoreValve (81) and Evolut R (149). The rate of device success was 81.7% among all patients. Of note, Evolute R showed a significantly higher rate of device success (86.9%) than CoreValve (72.2%). At 30 days, the rate of all-cause mortality was 13.3%, that of moderate AR was 9.1%, and that of severe AR was 1.4%. The rate of residual moderate/severe AR was significantly lower with Evolut R (19.1%) than CoreValve (6.3%). Multi-variable analysis revealed several risk factors correlated with mortality at 30 days, including the number of implanted valves, albumin < 3.3 mg/dL, and LVEF [24].

Takagi et al. have analyzed 911 patients undergoing TAVR for AR in 11 eligible studies in 2020. The total device success rate was found to be 80.4%, and NGDs were found to have a higher success rate (90.2%) than EGDs (67.2%). The study also found moderate to severe PVL in 7.4% of all patients, and indicated a lower rate with NGDs (3.4%) than EGDs (17.3%). In addition, the study reported a 30-day all-cause mortality rate of 9.5%, and indicated a lower rate with NGDs (6.1%) than EGDs (14.7%). The rate of mid-term (4 months to 1 year) all-cause mortality was 18.8%, and NGDs were associated with a lower mortality rate (11.8%) than EGDs (32.2%). Furthermore, life-threatening or major bleeding complications occurred in 5.7% of all patients, and the rate was lower for NGDs (3.5%) than EGDs (12.4%). Major vascular complications were reported in 3.9% of patients, and NGDs had a lower rate (3.0%) than EGDs (6.2%). All results indicated significantly better outcomes for NGDs than EGDs. Multivariable analysis identified >8% STS, major vascular complications, and moderate or higher PPA as independent risk factors associated with higher rates of 30-day mortality. Moreover, moderate or higher baseline MR, LVEF less than 45%, STS above 8%, acute kidney injury at stage 2 or higher, and moderate PPA were identified as independent risk factors for mortality at 1 year [33].

In 2022, Yin et al. studied 25 consecutive patients with PNAR who received new-generation THVs, which were compared with the early generation self-expanding CoreValve. The success rates were significantly higher (100% vs. 33%), and the rate of second valve implantation was lower (0% vs. 53%), for NGDs than EGDs. Patients who received NGDs rather than EGDs had higher rates of event-free survival during a median follow-up of 14 months, although the differences were not statistically significant (log-rank test, $P = 0.137$) [28]. Recently, Schneeberger et al. have reported the cases of nine patients with PNAR treated with self-expandable Acurate Neo and Neo2. The device success rate was 100%, and the early safety rate was 77.7%, owing to two cases of acute kidney injury (22.2%). At 30 days, the mortality rate was 0%. Trace levels of PVL were observed in 77.7% patients and was mild in 22.2%. No PPI was required [29]. Thus, the new device offers advantages in TAVR for PNAR.

In 2023, Koch et al. enrolled 125 patients, 91 receiving SAVR and 34 receiving TAVR. Patients who received TAVR had a significantly higher Society of Thoracic Surgeons predictive risk of mortality (STS-PROM) score than those in the SAVR group (3.96% vs. 1.25%). However, the in-hospital mortality and 30-day outcomes (including mortality, stroke, myocardial infarction, residual AR, or repeat valve intervention) did not differ between groups. The results indicated a significantly higher rate of complete heart block requiring PPI in the TAVR group (20.9% vs. 0%) [30].

Risk Factors Associated with Clinical Outcomes

Takagi et al. [33] have reported several factors negatively associated with mortality at 30 days for AR, including age, chronic obstructive pulmonary disease, peripheral arterial disease, LVEF, sex, hypertension,

atrial fibrillation, previous stroke, and pulmonary hypertension. Diabetes mellitus and concomitant moderate or higher MR were correlated with poor results in patients with AR treated with TAVR.

Furthermore, several studies have demonstrated that the number of valves implanted, albumin <3.3 mg/dL, longer intensive care unit stays, <20 kg/m^2 body mass index, >8% STS-PROM, major vascular complications, moderate or higher PPA, and low LVEF at baseline are associated with higher mortality at 30 days, and that moderate or higher baseline MR, LVEF <45%, STS-PROM >8%, acute kidney injury of stage 2 or higher, and moderate or severe PPA are associated with elevated 1-year mortality rates [20–22, 24, 28]. Moreover, new left bundle branch block and moderate to severe AR at discharge have been positively associated with NYHA functional class III or IV [21]. A larger annulus and a more dilated aorta are associated with less frequent device success [20].

Device embolization/migration are the main caveats to off-label use of TAVR devices designed for AR patients. De Backer et al. [22] have shown that relative device undersizing and oversizing are significantly associated with device embolization/migration and poorer clinical outcomes than TAVR with neutral THV sizing. All the risk factors associated with clinical outcomes were summarized in Table 2.

Guidelines and Clinical Management

On the basis of these trials, the 2021 European Society of Cardiology guidelines suggest that TAVR may be considered for selected patients with AR who are ineligible for SAVR and are treated at experienced centers. In clinical practice, the cardiac team must carefully choose patients with valvular calcification and annular sizes appropriate for a transcatheter approach (Figure 1). However, according to the current guidelines, SAVR remains the primary treatment option for symptomatic patients with substantial AR who have reduced left ventricular systolic function or severe LV dilatation [34, 35].

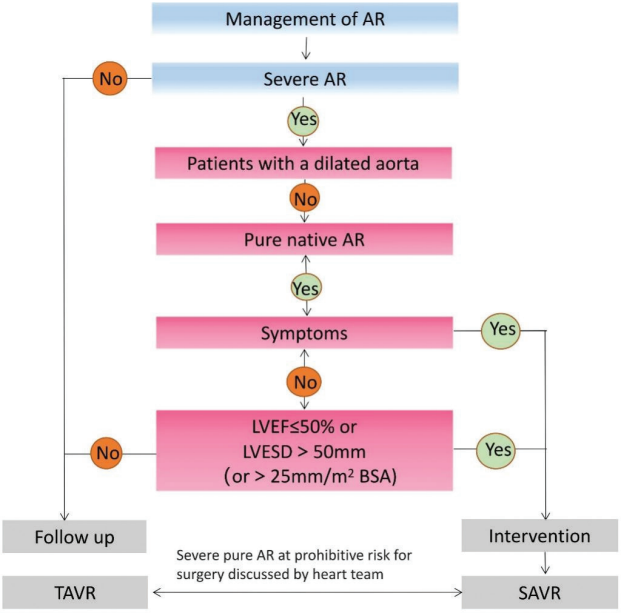

Figure 1 Treatment of Aortic Regurgitation.
BSA, body surface area; LVESD, left ventricle end-systolic diameter.

Tips for Performing TAVR in PNAR

The key points for performing TAVR in PNAR are as follows:

Table 2 Risk Factors Associated with Clinical Outcomes.

Outcomes	Risk factors
30-day mortality	Number of valves implanted, albumin < 3.3 mg/dL, longer intensive care unit stays, <20 kg/m^2 body mass index, >8% Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM), major vascular complications, moderate or higher post-procedural AR, low LVEF at baseline (Yoon et al. [20], Sawaya et al. [21], and De Backer et al. [22])
1-year mortality	Moderate or higher baseline MR, LVEF ≤ 45%, STS-PROM >8%, acute kidney injury at stage 2 or above, and moderate or higher post-procedural AR (Anwaruddin et al. [24] and Yin et al. [28])
NYHA functional class III or IV	Left bundle branch block and moderate to severe AR at discharge (Sawaya et al. [21])
Device success	Large annulus and dilated aorta (Yoon et al. [20])

(1) Careful pre-procedure multidetector computed tomography assessment should be performed to select the THV type, radiography position, approach vessels, etc.
(2) Ensuring that the position of THV is located at the right depth is essential to avoid THV malpositioning when the THV is released until it can start working. If the THV is malpositioned, it could be adjusted through the recycling delivery system.
(3) The THV release should follow the principle of "first slow and then fast": before the THV is anchored, the speed of THV release and the frequency of ventricular pacing must be carefully controlled. From the working position, to complete decoupling of the THV, appropriate ventricular pacing assistance and blood pressure control should be used to help stabilize the THV implantation. After the THV is fully released, and the THV adaptive position adjustment is manually controlled, the TIP part can be carefully removed.
(4) Several limiting factors must be considered before the procedure: First, approximately half of AR is due to aortic disease rather than valvular dysfunction, according to the etiology. Patients with annulus diameters >30 mm are not candidates for THV implantation, because of the coexistence of severe AR with pathological dilatation of the aortic root and ascending aorta. In addition, adequate and timely salvage strategies should be available for complications such as THV displacement or annulus rupture.

Clinical Case

A 74-year-old man with previous coronary artery disease and chronic obstructive pulmonary disease was admitted to our hospital because of dyspnea and syncope, and received an NYHA functional class III classification. Transthoracic echocardiograms revealed a PNAR with a central regurgitant jet, regurgitant volume of 55 mL/beat, regurgitation fraction of 50%, end-diastolic velocity of 20 cm/s, and diastolic flow reversal in the descending aorta. In addition, he had left ventricle dysfunction, with an LVEF of 45%.

Computed tomography angiography revealed a dilated aortic annulus (aortic annulus area of 613.2 mm^2 and aortic annulus perimeter of 89.6 mm) with no calcification of the annulus or leaflets (Figure 2). The ascending aorta diameter was measured to be 34.2 mm. The anatomy of the sinus of Valsalva, sinotubular junction, coronary arteries, and iliofemoral system was deemed suitable for TAVR.

After a thorough discussion among the heart team and consideration of the patient's high cardiac surgery risk (EuroSCORE II 21.15%, STS

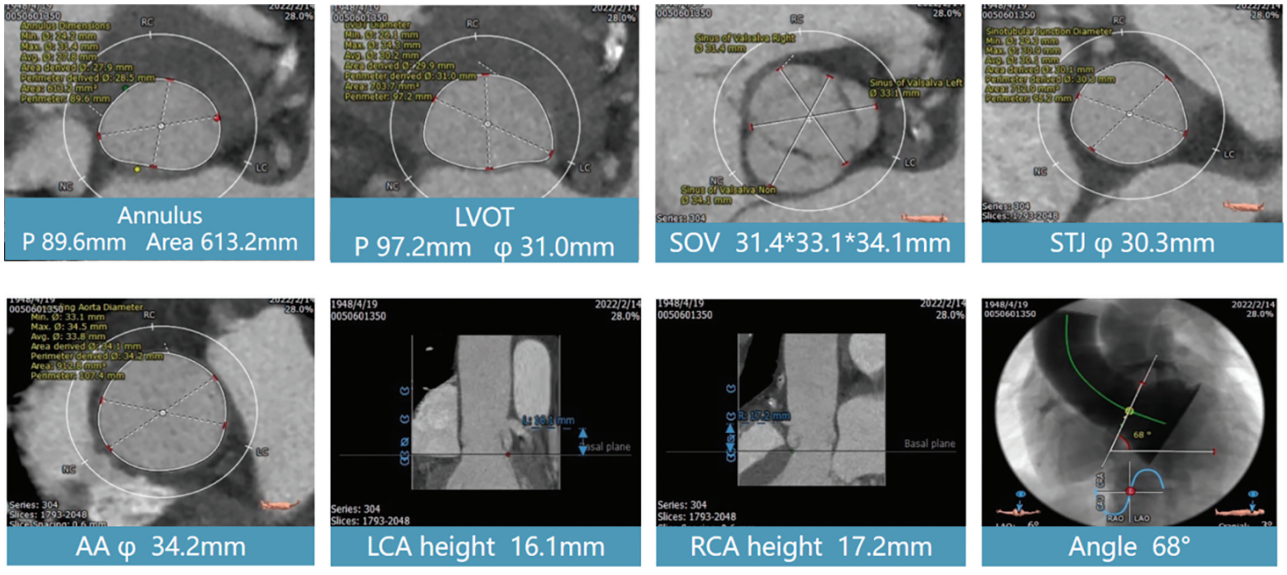

Figure 2 Preoperative CT Evaluation, Showing the Dilated Annulus (Area 613.2 mm^2, Perimeter 89.6 mm) and Normal Ascending Aorta Dimensions.

score 10.56%), we opted to proceed with a TAVR procedure using the self-expanding bioprosthesis (Vita Flow 30 mm) that was available at our center.

The procedure was performed with the patient under general anesthesia. A 5 F pigtail catheter was used to acquire an aortogram (a). The THV was carefully advanced until the aortic annulus was reached, and another aortogram was acquired to ensure proper THV positioning (b). Under pigtail guidance, the deployment was performed under rapid ventricular pacing (180 beats/min), with an extremely slow and careful technique without recapture, in a single attempt. When the THV was released to 2/3, an aortogram was acquired to ensure proper positioning (c). Then the THV was finally released, and a final contrast injection indicated proper prosthesis expansion, 3–5 mm implantation depth, no central or paravalvular leak, and coronary arteries with satisfactory flow (d). No rhythm disturbances were observed (Figure 3).

After the surgery, the patient's recovery proceeded smoothly without complications, and he was discharged home with no symptoms (NYHA functional class II). At the 30-day follow-up, an echocardiogram showed a well-functioning bioprosthesis with a mean aortic valve gradient of 9 mmHg and no residual aortic regurgitation.

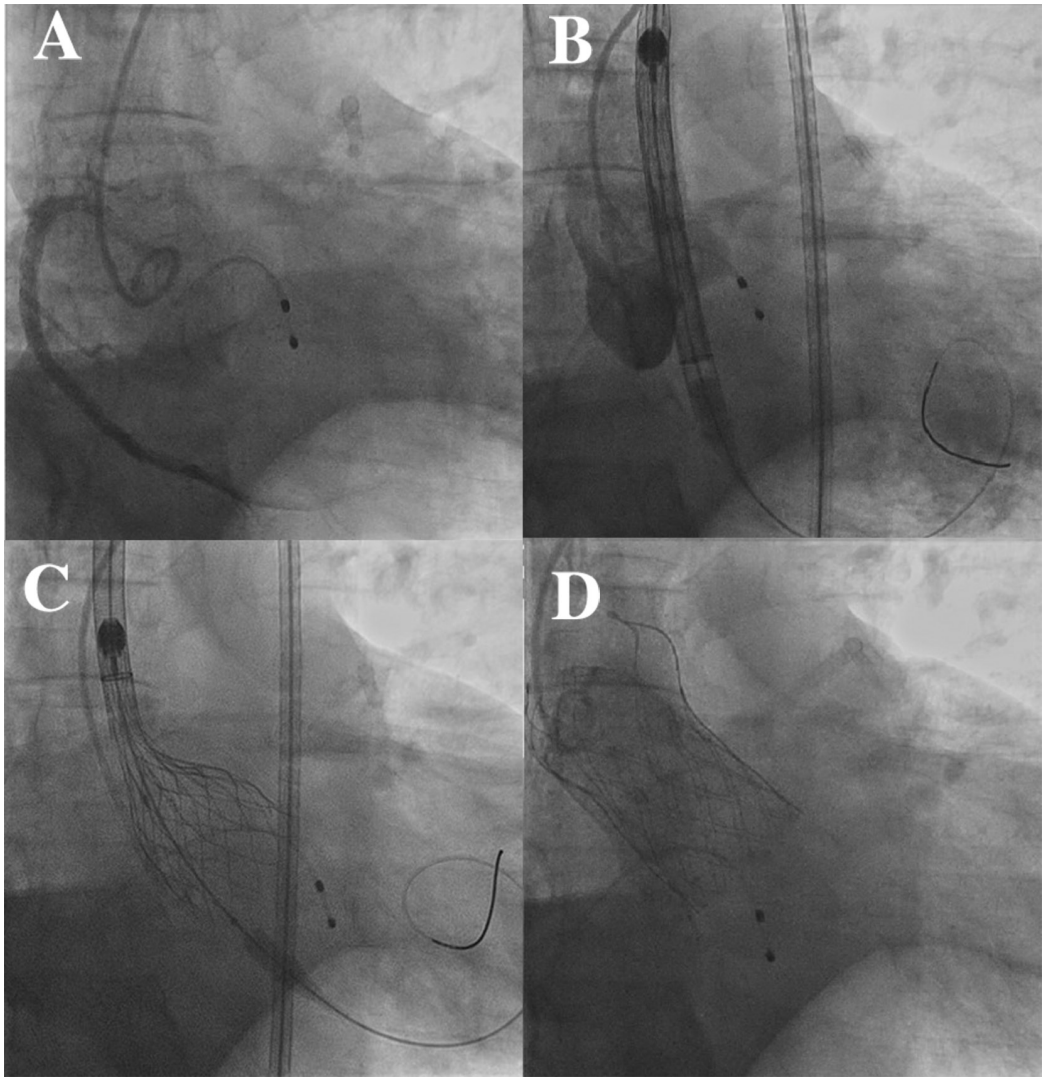

Figure 3 Procedural Steps of TAVR.
First, a pigtail catheter is positioned in the aortic sinuses of Valsalva (A). Subsequently, the transcatheter heart valve is initially deployed in position (B). Next, TAVR is slowly deployed under rapid ventricular pacing (C). Finally, the nose cone is removed with care, and the final deployment position is achieved (D).

Dedicated Device for AR

TAVR can be challenging because of aortic annulus and root dilation, as well as the absence of leaflet calcification, thus making device positioning and deployment difficult. Valve migration to the aorta or deep into the LV after implantation is associated with poor outcomes. Therefore, to decrease the risk of valve migration, valve oversizing has been proposed. Published studies recommend oversizing of 15–20% when selecting the THV size, but avoiding oversizing beyond 20% to avoid the risk of annular rupture and conduction abnormalities [21, 34].

Self-expandable THVs, such as the widely used CoreValve, have been the preferred non-specific devices for TAVR in cases of PNAR. These THVs can be retrieved and relocated, thus increasing predictability during the procedure [27, 31]. To date, several devices have been developed for pure AR, including JenaValve, J-valve, Acurate neo-2, Edwards HELIO, and Medtronic Engager.

The JenaValve™ was the first self-expanding device to receive the CE mark for NPAR (Figure 4). This valve is transapical and features three integrated locators, which enable precise placement in the native cusps and secure attachment of the THV onto the native leaflets [15, 16]. In 2017, a new generation transfemoral system was successfully used to treat PANR in the first case report in a human [19]. The JUPITER registry [36], which evaluated the long-term outcomes of the JenaValve, has reported a procedural success rate of 96.7%, with no incidence of valve malpositioning or of moderate to severe PPA. In a single-center experience with transfemoral access reported in 2020, 11 patients underwent TAVR with the JenaValve, and the device was implanted successfully in all cases [31]. In the 30-day follow-up, no instances of mortality or stroke were observed, and all patients showed amelioration of heart failure symptoms. The rate of PPI was 36.4%. In the 6-month follow-up, mild PVL was present in only one case, and PVL was observed at trace levels or was absent in the remaining patients.

The Trilogy Heart Valve System will be evaluated for safety and efficacy in high-risk patients diagnosed with severe AR through the ALIGN-AR trial, a single-arm, prospective study. The study's objective is to generate data supporting a future premarket approval submission to the U.S. Food and Drug

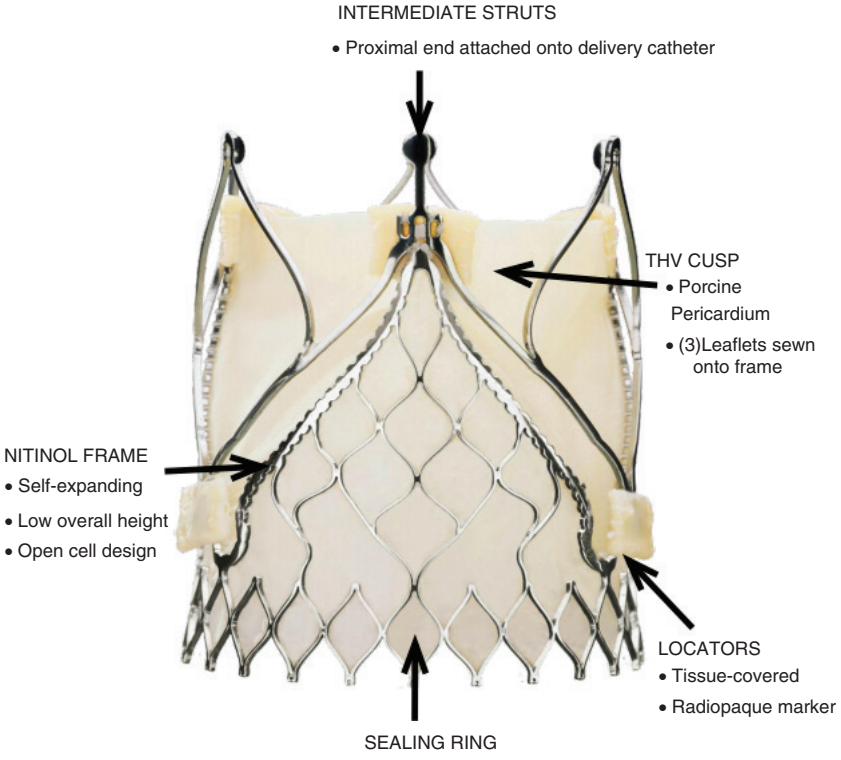

Figure 4 JenaValve™.

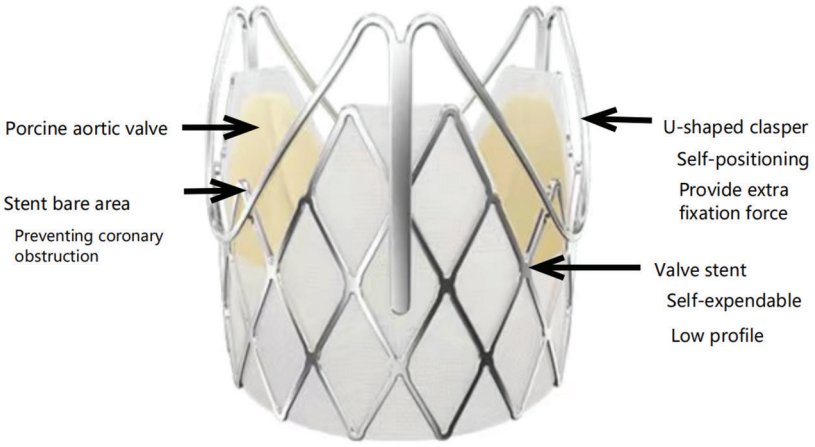

Figure 5 J-Valve™.

Administration. In patients with symptomatic AR at high surgical risk, transfemoral JenaValve implantation has been found to have a 95.7% success rate (68 of 71 patients), and mortality and stroke rates of 2.8% (2 of 71 patients) and 4.2% (3 of 71 patients), respectively, in 30-day follow-up [27]. The rate of PPI has been found to be 21.1% (15 of 71 patients), and PVL has been observed at absent or trace levels in 82% (58 of 71 patients), mild levels in 14% (10 of 71 patients), and mild-moderate levels in 4% (3 of 71 patients) of patients.

The J-Valve™ is another PNAR-dedicated second-generation device comprising a unique system composed of three U-shaped graspers, which facilitate intuitive self-positioning in implantation, and axial and radial fixation by embracing the native valve leaflets (Figure 5). A successful first-in-human implantation was reported in 2015. In a study by Liu et al. [23], the J-Valve was implanted through transapical access in 43 patients with severe PNAR who were at high surgical risk. The implantation was successful in 97.7% of cases (42/43), and the 1-year clinical outcomes included mortality (4.7%), disabling stroke (2.3%), and PPI (4.7%). After a 1-year follow-up, the rate of absent/trace postprocedural PVL was 76.9%, and that of mild PVL was 20.5%; the mean transvalvular gradient was 10.4 ± 4.5 mmHg. Li et al. have reported the 4-year outcomes of four patients with AR treated with the transapical J-valve. The mean gradient remained below 10 mmHg and did not significantly increase, and no residual valvular AR or PVL was detected [25]. In 2019, the first-in-human implantation of the transfemoral device was successfully performed [37], thus providing additional evidence supporting the safety and efficacy of dedicated AR devices through transfemoral access.

Future Directions

Patients with AR tend to be in poorer clinical condition than those with aortic stenosis, owing to irreversible LV dilatation and dysfunction. Although SAVR remains the standard intervention, TAVR has emerged as an alternative option for patients who have high risk or are inoperable. Although the anatomical and technical difficulties faced during the procedure make TAVR for NPAR an "off-label" treatment, experienced cardiac teams and dedicated devices have aided in overcoming these challenges. In recent clinical trials, NGDs and dedicated devices have achieved better results than EGDs, with lower rates of valve malpositioning, second valve implantation, and incidence of moderate to severe PPA.

Given that the anatomy of aorta is critical for the TAVR procedure, the AURORA study was designed to determine the morphological characteristics of the aortic root, to enforce the anchoring strength of THV [38]. Moreover, multiple ongoing trials worldwide are exploring device safety and efficacy in the TAVR procedure, such as the SEASON-AR (NCT 04864145) and SENSE-AR (NCT 05737264), RIVAL-AR EFS, and PANTHEON (NCT 05319171) trials. We look

forward to more studies that will benefit patients with AR by improving long-term outcomes, and filling knowledge gaps regarding interventional treatments in this field.

Author Contributions

RL and GS contributed to the initial idea for this study. RL, JY, YY, and GS were consulted about the clinical issues. RL, ZF, and GS contributed to the original draft. RL, ZF, JY, YY, and GS were responsible for the revision of the draft.

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Conflict of Interest

None declared.

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