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Original article

TAVI for aortic regurgitation using dedicated devices. A systematic review

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ABSTRACT

Introduction and objectives: Transcatheter aortic valve implantation (TAVI) for pure aortic regurgitation is challenging due to inadequate device anchoring and increased risks of device embolization and paravalvular regurgitation (PVR). This study aimed to review the safety and efficacy of TAVI for aortic regurgitation with devices specifically designed for this indication.
Methods: A comprehensive search of PubMed, Web of Science, Cochrane Library, and major conference archives up to April 2024 identified 143 unique results based on predefined criteria.
Results: Fifteen studies (n = 788 patients) were included, with J-Valve used in 357 patients and JenaValve in 431. Men represented 51% of the cohort, with a mean age of 74.7 ± 8.8 years and an STS-PROM score of 5.8 ± 4.9%. Transapical and transfemoral access routes were used in 62.7% and 37.3% of patients, respectively. Overall, procedural success was achieved in 95.9% of cases; surgical conversion was required in 1.8%, device migration/embolization occurred in 3.2%, and a second valve (in-valve) was required in 2.0% of patients. At 30 days, 95.5% of patients were alive, and device success was reported in 93.3% of cases. Mild PVR was observed in 18.0% of patients, moderate-to-severe PVR in 1.7%, and permanent pacemaker implantation (PPI) was required in 13.0%. In studies focusing on transfemoral procedures (all using JenaValve), the pooled estimates showed a procedural success rate of 97.8% (95%CI, 94.4-100), device success of 97.0% (95%CI, 94.8-99.2), 30-day mortality of 1.96% (95%CI, 0.20-3.72), moderate-to-severe PVR of 0.47% (95%CI, 0.00-1.47), and PPI requirement of 18.7% (95%CI, 13.9-23.4)
Conclusions: This systematic review of relatively small observational studies demonstrates the safety and favorable early outcomes of TAVI using J-Valve and JenaValve in patients with pure aortic regurgitation, especially when the transfemoral approach is used. Nevertheless, the need for PPI remains frequent.

Keywords: Aortic regurgitation. Transcatheter aortic valve implantation. Outcome. Systematic review. J-Valve. JenaValve.

TAVI para la regurgitación aórtica mediante dispositivos dedicados. Una revisión sistemática

RESUMEN

Introducción y objetivos: El implante percutáneo de válvula aórtica (TAVI) para la insuficiencia aórtica pura es un reto debido al anclaje inadecuado del dispositivo y al mayor riesgo de embolización de este y de regurgitación paravalvular (RPV). Nuestro objetivo fue revisar la seguridad y la eficacia del TAVI para la insuficiencia aórtica con dispositivos dedicados a esta indicación.
Métodos: Una búsqueda exhaustiva mediante criterios predefinidos en PubMed, Web of Science y Cochrane Library, así como en los principales archivos de congresos hasta abril de 2024, identificó 143 resultados únicos.
Resultados: Se incluyeron 15 estudios (n = 788 pacientes), en los que se utilizó J-Valve en 357 pacientes y JenaValve en 431. El 51% eran varones, la edad media fue de 74,7 ± 8,8 años y la puntuación STS-PROM fue de 5,8 ± 4,9%. Se utilizaron accesos transapicales y transfemorales en el 62,7 y el 37,3% de los casos respectivamente. En general, la intervención fue satisfactoria en el 95,9% de los casos; se requirió conversión quirúrgica en el 1,8%, se produjo migración/embolización del dispositivo en el 3,2%

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y fue necesaria una segunda válvula *(in-valve)* en el 2%. A los 30 días, el 95,5% de los pacientes estaban vivos y el éxito del dispositivo se alcanzó en el 93,3%. Se observó una RPV leve en el 18,0% y una RPV moderada-grave en el 1,7%, mientras que en el 13,0% fue necesario implantar un marcapasos permanente. En los estudios de intervenciones transfemorales (todas con JenaValve), la estimación conjunta del éxito de la intervención fue del 97,8% (IC95%, 94,4-100), del éxito del dispositivo fue del 97,0% (IC95%, 94,8-99,2), de la mortalidad a 30 días fue del 1,96% (IC95%, 0,20-3,72), de la RPV moderada-grave fue del 0,47% (IC95%, 0,0-1,47) y del implante de marcapasos permanente fue del 18,7% (IC95%, 13,9-23,4).
Conclusiones: Esta revisión sistemática de estudios observacionales relativamente pequeños demuestra la seguridad y los resultados precoces favorables del TAVI con J-Valve y JenaValve en pacientes con insuficiencia aórtica pura, en especial cuando se utiliza el abordaje transfemoral. No obstante, la necesidad de marcapasos permanente sigue siendo frecuente.

Palabras clave: Insuficiencia aórtica. Válvula aórtica percutánea. Resultados. Revisión sistemática. J-Valve. JenaValve.

Abbreviations

AoR: aortic regurgitation. **NYHA:** New York Heart Association. **PPI:** permanent pacemaker implantation. **PVR:** paravalvular regurgitation. **TAVI:** transcatheter aortic valve implantation.

INTRODUCTION

Aortic regurgitation (AR) results from abnormalities in the valve cusps or the structures supporting them (ie, the aortic root and annulus).[1] The prevalence of AR increases with age, affecting 2% of people older than 70 years.[2,3] Patients with severe AR have impaired functional capacity and increased mortality compared with the general population.[2,4]

If left untreated, severe AR leads to left ventricular dysfunction and heart failure in approximately 50% of patients.[2] Although surgical aortic valve replacement is the recommended treatment for symptomatic severe AR,[5] many elderly patients with this condition are refused surgery due to high operative risk.[6]

Since the introduction of transcatheter aortic valve implantation (TAVI) in 2002, it has demonstrated good safety and efficacy in various patient groups and several anatomical contexts.[7-13] However, due to the high stroke volume, the lack of aortic annular calcification, and the frequent dilatation of the aortic root/annulus, TAVI for pure native AR is associated with an increased risk of adverse events including device dislocation and paravalvular regurgitation (PVR).[14] The J-Valve(J.C. Medical, United States) and the JenaValve (JenaValve Technology GmbH, United States) are dedicated, next-generation, self-expanding transcatheter valves designed to address the challenges associated with native pure AR.[15,16]

To date, the evidence on the safety and efficacy of these technologies in native pure AR is limited. We conducted a systematic review of the current data on the safety and efficacy of TAVI using the J-Valve or JenaValve in patients with native pure AR.

METHODS

This systematic review and associated meta-analysis were conducted in accordance with the standards outlined in the PRISMA statement and the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0).[17,18] The study protocol was prospectively registered (PROSPERO registration number: CRD42023460306).

Data collection

We included studies that involved a minimum of 10 patients who underwent TAVI with the J-Valve or JenaValve for native pure or predominant AR. Studies were excluded if they involved mixed aortic valve disease (moderate to severe stenosis and regurgitation) or prior aortic valve replacement (valve-in-valve procedures).

Information sources, search strategy, and study selection

Three online databases (PubMed, Web of Science, and Cochrane Library) were searched up to March 2024 using the following search terms: ((aortic valve insufficiency OR aortic regurgitation OR regurgitant aortic valve OR aortic incompetency OR incompetent aortic valve OR NAVR OR noncalcific aortic valve) AND (transcatheter aortic valve replacement OR transcatheter aortic valve OR transfemoral aortic valve OR transaortic aortic valve OR transapical aortic valve OR transcutaneous aortic valve OR percutaneous aortic valve OR TAVI OR TAVR) AND (J-Valve OR JenaValve)). Additional relevant studies were identified through a manual search of secondary sources, including references of initially identified articles, reviews, commentaries, and archives of major cardiology conferences.

Endnote software (Clarivate Analytics, United States) was used to remove duplicates. The retrieved references were screened in 2 steps: first, all authors independently screened the titles and abstracts to determine their relevance, and second, the full-text articles of the identified abstracts were reviewed for final eligibility in the quantitative analysis. The Rayyan website was used in the selection process.[19] For overlapping study populations, the most recent publication was chosen for inclusion.

Data extraction and outcomes

The data were extracted into a standardized data extraction sheet, which included: *a)* study characteristics, *b)* the patients' baseline characteristics, c) echocardiographic and computed tomographic data, *d)* procedural data, and *e)* short-term clinical outcomes.

The main endpoints of the current investigation were device success, procedural success, and 30-day all-cause mortality. Additional outcomes of interest included bleeding, vascular complications, stroke, permanent pacemaker implantation (PPI), and PVR within 30 days.

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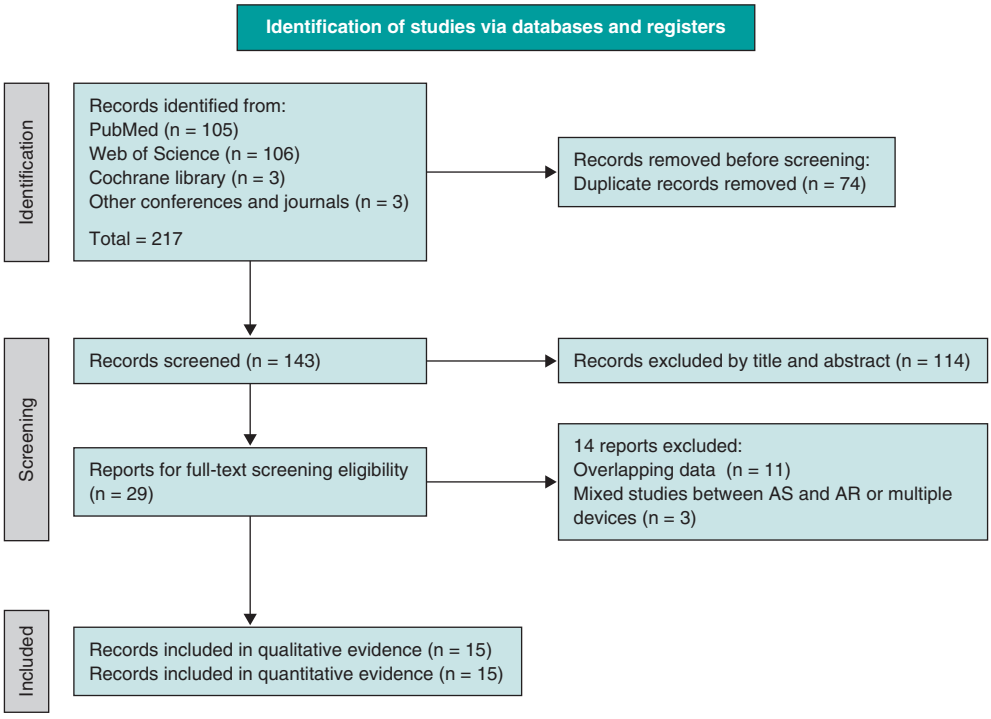

Figure 1. PRISMA flow diagram of the study.

Assessing the risk of bias

The quality of the retrieved studies was evaluated according to the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0, updated March 2011). The risk of bias was assessed using appropriate tools based on the study design: the National Institutes of Health (NIH) tool for single-arm observational studies, the Newcastle-Ottawa Scale (NOS) for comparative observational studies, and the NIH tool for case-series studies. The individual studies were classified as 'Low risk' or 'Good,' 'High risk' or 'Poor,' and 'Unclear risk' or 'Fair' of bias.

Assessment of heterogeneity

The statistical heterogeneity among the studies was assessed using the chi-square test, specifically the Cochrane Q test. The chi-square statistic, known as Cochrane Q, was used to compute the I-squared value using the following formula: $I2 = ([Q - df] / Q) \times 100\%$. Significant heterogeneity was defined as a chi-square P value < .1. An I-squared value equal to or more than 40% was considered indicative of a significant level of heterogeneity.

Quantitative analysis

The DerSimonian and Laird meta-analysis approach was used to obtain the pooled effect size for all outcomes. Proportions and 95% confidence intervals (95%CI) were computed using R software (version 4.3.1 for Windows) and the Meta package.

A random-effects model, which gives relatively higher weight to smaller studies to account for heterogeneity, was used when heterogeneity was deemed significant. A fixed-effects model was chosen when heterogeneity was lower. Consequently, the predicted effects in our meta-analysis are conservative estimates that account for potential inconsistencies.

Certainty assessment

A certainty evaluation was performed using sensitivity analysis (leave-one-out meta-analysis) to test the robustness of the evidence. This analysis was conducted using R software (version 4.3.1 for Windows) with the Meta package and Metainf function. Sensitivity analyses were was run in several scenarios for each outcome in the meta-analysis, eliminating one study in each scenario, to ensure that the overall effect size was not dependent on any single study.

RESULTS

Literature search

Our search identified 143 results after duplicates were removed. Following title and abstract screening, 29 articles were selected for full-text review. Of these, 15 studies[6,14,20-32] were included in the systematic review, with 5 studies of transfemoral TAVI being included in the quantitative meta-analysis. No further articles were included after manually searching the references of the included studies. The selection process is illustrated in a PRISMA flow diagram (figure 1). According to the NIH and NOS scales for quality assessment, the overall quality of the included studies was rated as good for all investigations, as shown in the supplementary data.

Patient and procedural characteristics

Overall, 788 patients underwent TAVI for native pure or predominant AR (J-Valve, 357 patients; JenaValve, 431 patients). Most J-Valve procedures were performed in China, while most JenaValve procedures were conducted in Europe and North America. The average surgical risk was elevated but showed significant variability, with Log EuroSCORE at 22.8 ± 12.3, EuroSCORE II at 7.1 ± 6.6, and Society of Thoracic Surgeons - Predicted Risk of Mortality (STS-PROM) at 5.9 ± 4.7.

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The mean age was 73.6 ± 7.3 years for J-Valve recipients and 75.9 ± 10.0 years for JenaValve recipients. Males comprised 61.9% of J-Valve recipients and 42.0% of JenaValve recipients. The body mass index (BMI) was 22.6 ± 3.0 for J-Valve recipients and 25.3 ± 5.7 for JenaValve recipients. The STS-PROM score was 6.7 ± 5.9 for J-Valve recipients and 4.4 ± 3.5 for JenaValve recipients. Most patients had severe symptoms, with New York Heart Association (NYHA) class III/IV dyspnea present in 75.9% of J-Valve recipients and 57.3% of JenaValve recipients. Demographic, clinical, echocardiographic, and computed tomography data from the individual studies are summarized in table 1 and table 2.

Most J-Valve implantations were performed via the transapical approach (92.4%), whereas JenaValve implantations were transapical in 36.7% of cases and transfemoral in 63.3%. The annulus diameter was 26.0 ± 2.4 mm for J-Valve and 25.6 ± 2.3 mm for JenaValve. The device size was 27.2 ± 1.9 mm for J-Valve and 26.1 ± 0.2 mm for JenaValve. The most frequently used device size was 27 mm. Further procedural data from the individual studies are summarized in table 3.

In-hospital outcomes

Overall, in-hospital outcomes were favorable. Procedural success was achieved in 95.9% (n = 518/540). Surgical conversion was required in 1.8% (n = 12/678), device migration or embolization occurred in 3.2% (n = 17/540), and a second valve (in-valve) was required in 2.0% (n = 13/651). Only 1 patient (out of 502) experienced coronary obstruction, and no patients developed annular rupture (among 449). Details of in-hospital outcomes from the individual studies are summarized in table 4.

Thirty-day outcomes

At 30 days, 95.5% of patients were alive (n = 716/750), and device success was achieved in 93.3% (n = 498/534). Mild PVR was observed in 18.0% (n = 86/478), while moderate-to-severe PVR occurred in 1.7% (n = 12/703; including 10 patients with J-Valve and 2 patients with JenaValve). PPI was required in 13.0% (n = 86/711; with 25 patients receiving J-Valve and 61 receiving JenaValve). Further 30-day outcomes from the individual studies are summarized in table 5.

Quantitative analysis of the outcomes of transfemoral TAVI for aortic regurgitation

A meta-analysis of 5 studies[25-28,32] of transfemoral TAVI for AR (all with the JenaValve) included 273 patients (mean age, 77.6 years; 52.4% male). Pooled estimates were as follows: procedural success was 97.8% (95%CI, 94.4%-100%, I^2 = 43%, *P* value = .13) (figure 2A), conversion to surgery was 0.49% (95%CI, 0.0%-1.5%, I^2 = 0%, *P* value = .56) (figure 2B), device migration/embolization was 1.2% (95%CI, 0.0-3.3%, I^2 = 47%, *P* value = .17) (figure 2C), and the need for a second valve was 0.46% (95%CI, 0.0%-1.44%, I^2 = 0%, *P* value = .67) (figure 2D). Further details of in-hospital outcomes are summarized in table 6 and in the supplementary data.

At 30 days, the pooled estimate of device success was 97.0% (95%CI, 94.8%-99.2%, I^2 = 0%, *P* value = .61) (figure 3A), and the pooled estimate of all-cause mortality was 2.0% (95%CI, 0.2%-3.7%, I^2 = 0%, *P* value = .95) (figure 3B). The rate of PPI was 18.7% (95%CI, 13.9%-23.4%, I^2 = 0%, *P* value = .58) (figure 3C). Mild PVR rate was 10.6% (95%CI, 1.7%-19.4%, I^2 = 75%, $P < .01$) (figure 4A) with statistically significant heterogeneity resolved by omitting Vahl et al.[32] yielding a rate of 4.7% (95%CI, 0.0%-9.5%, I^2 = 38%) (supplementary data), while the rate of moderate-severe PVR was 0.47% (95%CI, 0.0%-1.47%, I^2 = 0%, *P*- = 1.00) (figure 4B). Further 30-day outcomes are summarized in table 7 and in the supplementary data.

DISCUSSION

In this study, we included data from 788 patients who underwent TAVI using 1 of the 2 dedicated devices specifically designed for use in pure/predominant AR: the J-Valve and the JenaValve (figure 5). Studies published up to April 2024 were included, providing a contemporary and comprehensive analysis of published data in this field to date. Overall, 357 patients received the J-Valve (in 5 studies), while 431 received the JenaValve (in 10 studies). These patients were generally at increased surgical risk. J-Valve recipients were predominantly Chinese, tended to be slightly younger, had a smaller BMI, wand showed a clear male predominance compared with JenaValve recipients.

The use of the 2 technologies (J-Valve and JenaValve) was influenced by their geographical availability, leading to differences between the populations treated with each device. Moreover, as mentioned earlier, the 2 groups differed in age, sex, and STS-PROM scores. Additionally, most of the transfemoral implantations involved the JenaValve, while the vast majority of J-Valve implantations were transapical. Consequently, direct statistical comparison between the 2 devices and the 2 access routes was deemed inappropriate. For similar reasons, we avoided pooling data from all JenaValve procedures (mixing transapical and transfemoral implantations) and from all transapical procedures (mixing J-Valves and JenaValves). This approach minimized the risk of drawing invalid conclusions by mixing heterogeneous data or comparing outcomes without accounting for important independent confounders. Patients receiving the JenaValve via the transfemoral approach constituted a homogeneous subgroup, allowing for pooled/quantitative analysis. The findings of this latter analysis are particularly important, as transfemoral access currently dominates the TAVI field.

Our systematic review combines prospective and retrospective studies, which share common limitations such as small sample sizes and nonrandomized designs. Therefore, the findings should be regarded as preliminary and require validation in larger randomized studies. From the available data, our major observations can be summarized as follows: first, TAVI using AR-dedicated devices demonstrated a high success rate with a reassuring early safety profile. Second, the rates of surgical conversion, device dislocation, and second valve implantation were low (2%-3%). Third, both dedicated devices effectively eliminated or reduced AR, with only 1% to 2% of patients having ≥ moderate residual AR. Fourth, the results of transfemoral TAVI for AR using the JenaValve were particularly encouraging, although the PPI rate was still relatively high. Taken together, these initial findings suggest that transcatheter treatment of AR, especially through transfemoral access, may be a safe and effective alternative to surgery in appropriately selected patients.

Treating AR with TAVI using the first/older generations of transcatheter heart valves has been associated with suboptimal results.[35,36] However, subsequent studies showed that next/newer generation transcatheter heart valves can improve outcomes, bringing them closer to those achieved in patients with AS.[13] With the introduction of dedicated devices, several key outcomes have shown further improvement, yielding very high procedural and device success rates and low rates of conversion to surgery, device migration or embolization, the need for a second valve, and PVR. Although annular injury is a concern given the frequent association of AR with

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Table 1. Baseline characteristics of patients included in 15 unique studies

Study ID	Countries	Recruitment	Device	Approach	Patient n	Male	Age	BMI (kg/m^2)	EuroSCORE I	EuroSCORE II	STS-PROM	NYHA III/IV	HTN
Garcia et al.[20] 2023	USA, Canada	May 2018 - Oct 2022	J-Valve	TF[a]	27	16 (59)	79.3 ± 9.6	-	-	-	4.1 ± 2.0	26 (96.3)	24 (89)
Kong et al.[21] 2022	China	Sept 2016 - Sept 2022	J-Valve	TA	69	52 (75.4)	71.5 ± 7.9	22.70 ± 3.15	-	-	3.8 ± 3.9	53 (76.8)	48 (69.6)
Liu et al.[b,22] 2022	China	March 2014 - June 2019	J-Valve	TA	161	119 (73.9)	72.5 ± 6.2	-	-	-	9.9 ± 5.7	157 (98.1)	107 (66.5)
Huan Liu et al.[23] 2020	China	May 2014 - October 2018	J-Valve	TA	47	34 (72.3)	73.7 ± 7.9	22.6 ± 2.9	24.3 ± 5.1		-	35 (74.5)	31 (66.0)
W. Liu et al.[24] 2019	China	June 2017 - December 2018	J-Valve	TA	53	-	76.4 ± 5.2	-	-	-	6.3 ± 1.8	-	-
Vahl et al.[32] 2024	USA (20 sites)	June 8, 2018 - Aug 29, 2022	JenaValve	TF	180	95 (53)	75.5 ± 10.8	25.3 ± 6.1	-	-	4.1 ± 3.4	122 (68)	149 (83)
Adamet al.[25] 2023	Germany (6 centers)	Sept 2021 - July 2022	JenaValve	TF	58	37 (63.8)	76.5 ± 9.0	26.19 ± 4.36	-	6.10 ± 6.60	4.2 ± 4.3	43 (74)	53 (91)
Baumbach et al.[26] 2023	UK	-	JenaValve	TF	12	7 (58)	83.3 ± 6.7	-	-	-	4.6 [4.1-6.6]	11 (92)	8 (67)
Ranard et al.[27] 2022	USA	July 2018 - March 2020	JenaValve	TF	11	-	77.6 ± 8.9	-	-	-	-	-	-
Baldus et al.[28] 2019	Germany and Netherlands (7 centers)	-	JenaValve	TF	12	4 (33.3)	75 ± 7.2	-	-	-	3.5 ± 2.1	8 (67)	-
Silaschi et al.[29] 2018	Germany (15 center)	2012 - 2015	JenaValve	TA	30	12 (40.0)	74.4 ± 9.3	-	17.7 ± 14.8	6.9 ± 6.5	4.9 ± 3.5	27 (90)	24 (80.0)
Sawaya et al.[14] 2017	Europe, North America, and Asia Middle East (18 center)	July 2007 - Sept 2016	JenaValve[c]	TA	23/146	-	-	-	-	-	-	-	-
Yoon et al.[6] 2017	Europe, North America, and Asia	Sept 2007 - Feb 2017	JenaValve[d]	TA[e]	64/212	-	-	-	-	-	-	-	-
Seiffert et al.[30] 2014	9 centers, Germany	April 2012 - October 2013	JenaValve	TA	31	20 (64.5)	73.8 ± 9.1	24.0 ± 4.5	23.6 ± 14.5	9.3 ± 6.4	5.4 ± 3.6	28 (90.3)	26 (83.9)
Schlingloff et al.[31] 2014	Hamburg, Germany	December 2012 - Sept 2013	JenaValve	TA	10	6 (60)	79.1 ± 9.3	-	28.3 ± 17.1	-	7.0 ± 1.0	9 (90)	-

(Continues)

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Table 1. Baseline characteristics of patients included in 15 unique studies *(continued)*

Study ID	DM, No. (%)	COPD, No. (%)	AF, No. (%)	PVD, No. (%)	Chronic renal disease, No. (%)	Prior pacemaker, No. (%)	Cerebrovascular disease, No. (%)	Pulmonary hypertension, No. (%)	CAD, No. (%)	Prior MI, No. (%)	Prior PCI, No. (%)	Prior CABG, No. (%)
Garcia et al.[20] 2023	5 (19)	7 (26)	12 (44)	4 (15)	NA	3 (11)	4 (15)	-	-	4 (15)	13 (48)	4 (15)
Kong et al.[21] 2022	9 (13.0)	14 (20.3)	18 (26.1)	7 (10.1)	5 (7.2)	2 (2.9)	6 (8.7)	-	19 (27.5)	0	4 (5.8)	1(1.4)
Liu et al.[b,22] 2022	24 (14.9%)	50 (31.1)	36 (22.4)[f]	-	34 (21.1)	5 (3.1)	51 (31.7)	53 (32.9)	52 (32.3)	-	4 (2.5)	-
Huan Liu et al.[23] 2020	4 (8.5)	9 (19.1)	9 (19.1)	10 (21.3)	-	1 (2.1)	15 (31.9)	-	11 (23.4)	0 (0)	2 (4.3)	2 (4.3)
W. Liu et al.[24] 2019	-	-	-	-	-	-	-	-	-	-	-	-
Vahl et al.[32] 2024	26 (14)	32 (18)	72 (40)	21 (12)	58 (33)	30 (16)	19 (11)	-	-	-	37 (23)	20 (12)
Adamet al.[25] 2023	14 (24)	9 (16)	34 (59)	7 (12)	-	7 (12)	8 (14)	-	25 (43)	5 (8.6)	17 (29)	-
Baumbach et al.[26] 2023	1 (8)	2 (17)	7 (58)	-	4 (33)	-	2 (17)	-	-	-	2 (17)	
Ranard et al[27] 2022	-	-	-	-	-	-	-	-	-	-	-	-
Baldus et al.[28] 2019	-	-	5 (42)	-	-	-	-	3 (25)	-	-	2 (17)	-
Silaschi et al.[29] 2018	5 (16.7)	5 (16.7)	9 (30.0)	3 (10.0)	11 (36.7)	4 (13.3)	2 (6.7)	10 (33.3)	14 (46.7)	1 (3.3)	8 (26.7)	5 (16.7)
Sawaya et al.[14] 2017	-	-	-	-	-	-	-	-	-	-	-	-
Yoon et al.[6] 2017	-	-	-	-	-	-	-	-	-	-	-	-
Seiffert et al.[30] 2014	4 (12.9)	9 (29.0)	6 (19.3)	6 (19.3)	-	3 (9.7)	6 (19.3)	6 (20)	20 (64.5)	11 (35.5)	10 (32.2)	7 (22.6)
Schlingloff et al.[31] 2014	-	-	-	-	-	-	-	-	-	-	-	-

AF, atrial fibrillation; AS, aortic stenosis; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic (obstructive) pulmonary disease; DM, diabetes mellitus; EuroSCORE, European System for Cardiac Operative Risk Evaluation; HTN, hypertension; MI, myocardial infarction; NYHA, New York Heart Association; PVD, peripheral vascular disease; PCI, percutaneous coronary intervention; STS-PROM, Society of Thoracic Surgeons Predicted Risk Of Mortality; TA, transapical; TF, transfemoral.

The data are presented as mean ± standard deviation, median [IQR], or No. (%).

[a] F in 21. Other access: 1 carotid, 4 subclavian, 1 transcaval.

[b] Liu et al.[22] (2022) included 29 (18.0%) patients with concomitant mild AS and 1 patient (0.6%) with bioprosthetic valve failure.

[c] Sawaya et al.[14] (2017) included different devices; the number of JenaValve recipients was 23.

[d] Yoon et al.[6] (2017) included different devices, but number of JenaValve patients was 64.

[e] Yoon et al.[6] (2017) included 63 transapical implantations.

[f] Atrial fibrillation/flutter.

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Table 2. Echocardiographic and computed tomographic data

Study ID	LVEF (%)	LVEDD (mm)	MR, ≥ moderate	Aortic regurgitation grade		Bicuspid AV	Ascending aorta diameter	Aortic annulus diameter	Aortic annulus perimeter
				Moderate	Severe				
Garcia et al.[20] 2023	54 [37–60]	55 ± 90	-	5 (19)	22 (81)	1 (4)	-	25.6 ± 3	81 ± 10.5
Kong et al.[21] 2022	50.8 ± 12.4	-	-	69 (100)		-	-	-	-
Liu et al.[b,22] 2022	52.3 ± 12.8	65.1 ± 9.3	-	-	161 (100)	13 (8.1)	41.4 ± 5.2	26.2 ± 2.4	-
Huan Liu et al.[23] 2020	52.3 ± 12.4	59.2 ± 8.4	5 (10.6)	0	47 (100)	3 (6.4)	40.1 ± 4.9	27.1 ± 2.2[a]	-
W. Liu et al.[24] 2019	-	-	-	0	53 (100)	-	-	-	-
Vahl et al.[32] 2024	53.8 ± 11.4	-	-	5 (3)	116 (64)	-	37·3 ± 5·0	-	79·1 ± 6·1
Adamet al.[25] 2023	-	-	25 (43.1)[b]	2 (3.4)	56 (96.6)[c]	-	-	-	80.3 ± 9.7
Baumbach et al.[26] 2023	47 [39–56]	60 [59–66]	-	-	12 (100)	-	-	27 × 24[d]	-
Ranard et al[27] 2022	44.6 ± 10.4	64 ± 8	-	11 (100)		-	-	-	-
Baldus et al.[28] 2019	53.0 ± 8.5	-	10 (83)	-	12 (100)	-	-	25 ± 2.3	-
Silaschi et al.[29] 2018	49.6 ± 13.3	-	15 (50)	1 (3.3)	29 (96.7)	-	-	24.3 ± 1.9	-
Sawaya et al.[14] 2017	-	-	-	-	-	-	-	-	-
Yoon et al.[6] 2017	-	-	-	-	-	-	-	-	-
Seiffert et al.[30] 2014	46.8 ± 16.1	-	8 (25.8)	1 (3.2)	30 (96.8)	-	36.6 ± 7.0	24.7 ± 1.5	-
Schlingloff et al.[31] 2014	48.2 ± 15.8	62 ± 2.2	3 (30)	-	10 (100)	-	-	-	-

AR, aortic regurgitation; Bicuspid AV, bicuspid aortic valve; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; MR, mitral regurgitation.
The data are presented as mean ± standard deviation, No. (%), or median [IQR].
[a] Perimeter-derived diameter.
[b] Including mild to moderate MR.
[c] Including moderately-severe and severe AR.
[d] Data presented as median.

Table 3. Procedural characteristics

Study ID	Device	Access	Valve prosthesis size (mm)					Average prosthesis size, mm	BPostD
			21 mm	23 mm	25 mm	27 mm	29 mm		
Garcia et al.[20] 2023	J-Valve	TF[a]	-	-	-	-	-	26.9 ± 1.8	0 (0)
Kong et al.[21] 2022	J-Valve	TA	-	-	-	-	59 (85.9)	29[c]	-
Liu et al.[b,22] 2022	J-Valve	TA	4 (2.5)	15 (9.3)	35 (21.7)	64 (39.75)	43 (26.7)	26.6 ± 2.0	-
Huan Liu et al.[23] 2020	J-Valve	TA	-	1 (2.1)	7 (14.9)	26 (55.3)	13 (27.7)	27.2 ± 1.4	0 (0)
W. Liu et al.[24] 2019	J-Valve	TA	-	-	-	-	-	-	-
Vahl et al.[32] 2024	JenaValve	TF	-	40 (23)	35 (20)	102 (58)	-	25.7 ± 1.6	7 (4)
Adamet al.[25] 2023	JenaValve	TF	-	4 (6.9)	16 (27.6)	38 (65.5)	-	26.2 ± 1.2	2 (3.4)
Baumbach et al.[26] 2023	JenaValve	TF	-	-	3 (25)	9 (75)	-	26.5 ± 0.9	-
Ranard et al[27] 2022	JenaValve	TF	-	-	-	-	-	-	-
Baldus et al.[28] 2019	JenaValve	TF	-	2 (16.7)	2 (16.7)	8 (66.7)	-	26 ± 1.6	0 (0)
Silaschi et al.[29] 2018	JenaValve	TA	-	4 (13.3)	11 (36.7)	15 (50.0)	-	25.7 ± 1.4	1 (3.3)
Sawaya et al.[14] 2017	JenaValve	TA	-	-	-	-	-	-	-
Yoon et al.[6] 2017	JenaValve	TA[b]	-	-	-	-	-	-	-
Seiffert et al.[30] 2014	JenaValve	TA	-	4 (12.9)	7 (22.6)	20 (64.5)	-	26.3 ± 1.5	2 (6.4)
Schlingloff et al.[31] 2014	JenaValve	TA	-	1 (10)	2 (20)	7(70)	-	26.2 ± 1.4	-

AVPG, aortic valve pressure gradient; BPostD, balloon postdilatation.
The data are presented as mean ± standard deviation or No. (%).
[a] Transfemoral in 21. Other access: 1 carotid, 4 subclavian, 1 transcaval.
[b] Transapical in 63/64.
[c] Data presented as mean.

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Table 4. In-hospital outcomes

Study ID	Procedural success		Conversion to surgery		Coronary obstruction		Annulus rupture		Device migration/ embolization		Need for second valve		Bleeding, major or life-threatening		Vascular and access-related complications		Acute kidney injury		In-hospital mortality	
	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total
Garcia et al.[20] 2023	22 (81)	27	2 (7)	27	-	-	-	-	3 (11.1)	27	3 (11.1)	27	-	-	5(18.5)	27	-	-	1 (3.7)	-
Kong et al.[21] 2022	67 (98.5)	68	1 (1.4)	69	-	-	-	-	1(1.4)	68	-	-	5 (7.4)	68	-	-	-	-	0 (0)	68
Liu et al.[b,22] 2022	-	-	4 (2.5)	161	1 (0.6)	161	0 (0)	161	4 (2.5)	161	0 (0)	161	1 (0.6)	161	-	-	-	-	3 (1.9)	161
Huan Liu et al.[23] 2020	46 (97.9)	47	0 (0)	47	0 (0)	47	0 (0)	47	1(2.1)	-	1 (2.1)	47	0	47	0 (0)	47	8(17.0)	47	-	-
W. Liu et al.[24] 2019	51 (96.2)	53	2 (3.8)	53	0 (0)	53	-	-	2 (3.8)	53	1 (1.9)	53	5 (14.3)	53	-	-	-	-	-	-
Vahl et al.[32] 2024	171 (95)	180	1 (< 1)	180	0 (0)	180	0 (0)	180	4(2.2)	180	1 (< 1)	180	8 (4)	180	7 (4)	180	2 (1)	180	0 (0)	180
Adamet al.[25] 2023	58 (100)	58	0 (0)	58	-	-	-	-	0 (0)	58	0 (0)	58	0 (0)	58	4 (6.9)	58	7 (12)	58	0 (0)	58
Baumbach et al.[26] 2023	12 (100)	12	-	-	-	-	-	-	-	-	-	-	1 (8.3)	12	5(41.7)	12	1 (8.3)	12	-	-
Ranard et al.[27] 2022	11 (100)	11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Baldus et al.[28] 2019	11 (92)	12	1 (8.3)	12	-	-	-	-	-	-	-	-	-	-	1 (8.3)	12	-	-	0 (0)	12
Silaschi et al.[29]2018	29 (96.7)	30	1 (3.7)	27	0 (0)	30	0 (0)	30	1 (3.3)	30	0	30	1 (3.3)	30	1 (3.3)	30	0 (0)	30	-	-
Sawaya et al.[14] 2017	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2(8.7)	23	-	-	-	-
Yoon et al.[6] 2017	-	-	-	-	-	-	-	-	-	-	6 (9.4)	64	5 (7.8)	64	1 (1.6)	64	4 (9.4)	47	-	-
Seiffert et al.[30] 2014	30 (96.8)	31	0 (0)	31	0 (0)	31	0 (0)	31	1 (3.2)	31	1 (3.2)	31	3 (9.7)	31	4 (13)	31	7 (22.5)	31	-	-
Schlingloff et al.[31] 2014	10 (100)	10	0 (0)	10	-	-	-	-	-	-	-	-	0 (0)	10	-	-	-	-	0 (0)	10

AR, aortic regurgitation.
The data are presented as No (%).

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Table 5. Thirty-day outcomes

Study ID	Device success		30-day all-cause mortality		30-day Stroke		30-day PPI		30-day mild PVR		30-day PVR ≥ moderate		30-day EOA (cm^2)	30-day mean AV PG	30-day repeat procedure for valve-related dysfunction		NYHA class III/ IV	
	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total	Event	Total			Event	Total	Event	Total
Garcia et al.[20] 2023	-	-	1 (4)	24	1 (4)	24	3 (13)	24	8 (33)	24	0 (0)	24	2.1 ± 0.6	7 ± 4	-	-	3 (12)	24
Kong et al.[21] 2022	-	-	1 (1.5)	68	2 (2.9)	68	5 (7.5)	67	19 (28)	68	4 (5.9)	68	-	-	-	-	7 (10)	68
Liu et al.[b,22] 2022	153 (95.0)	161	3 (1.9)	161	1 (0.6)	161	13 (8.3)	155	-	-	4 (1.9)	161	-	8.5 ± 2.9	1 (0.6)	161	1 (0.6)	161
Huan Liu et al.[23] 2020	-	-	1 (2.1)	47	0 (0)	47	2 (4.3)	46	14(30.4)	47	1 (2.1)	47	-	7.9 ± 2.4	0 (0)	47	2 (4.5)	44
W. Liu et al.[24] 2019	-	-	5 (9.2)	53	0 (0)	53	2 (5.7)	53	3 (5.6)	53	1 (1.9)	53	-	-	-	-	-	-
Vahl et al.[32] 2024	174 (96.7)[b]	180	4 (2)	180	4 (2)	180	36 (24)	180[a]	31 (19)	180	1 (0.6)	180	2.8 ± 0.6[e]	3·9 ± 1·6	-	-	16 (9)	180
Adamet al.[25] 2023	47 (98)	48	1 (1.7)	58	0 (0)	57	10 (19.6)	51	2 (4.1)	49	0 (0)	49	2.65 ± 0.6[c]	4.5 ± 2.0	-	-	4 (7.7)	52
Baumbach et al.[26] 2023	-	-	0 (0)	12	-	-	2 (17)	12	3 (33)	12	0	12	-	-	-	-	3 (25)	12
Ranard et al.[27] 2022	-	-	-	-	-	-	-	-	0 (0)	11	0 (0)	11	2.7 ± 0.4	4.1 ± 1.7	-	-	-	-
Baldus et al.[28] 2019	-	-	0 (0)	12	0 (0)	12	1 (8.3)	12	2 (20)	10	0 (0)	10	2.4 ± 0.5	4.3 ± 1.7	-	-	0 (0)	9
Silaschi et al.[29] 2018	24 (88.9)	27	3 (10.0)	30	1 (3.3)	30	1 (3.8)	26	4 (15.4)	26	0 (0)	26	-	11.4 ± 3.7[d]	1 (3.3)	30	11 (41)	27
Sawaya et al.[14] 2017	18 (78.2)	23	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Yoon et al.[6] 2017	52 (82.8)	64	8 (12.5)	64	5 (7.8)	64	7 (15.8)	47	-	-	1 (1.6)	64	-	-	-	-	-	-
Seiffert et al.[30] 2014	30 (96.8)	31	4 (12.9)	31	0 (0)	31	2 (71.4)	28	-	-	-	-	-	7.9 ± 4.0[d]	-	-	4 (15.3)	26
Schlingloff et al.[31] 2014	-	-	3 (30)	10	-	-	2 (20)	10	0 (0)	6	0 (0)	6	-	7.2 ± 4.3	-	-	0 (0)	10

EOA, effective orifice area; NYHA, New York Heart Association; PPI, permanent pacemaker; PVR, prosthetic valve regurgitation.
The data are presented as No. (%).
[a] 30 patients had a previous pacemaker.
[b] Data of device success reported in the abstract presented in TCT 2023. Makkar et al.[33] 2023.
[c] Assessed at discharge.
[d] Immediate postprocedural measurement.
[e] Data of EOA mentioned in the abstract published in JAAC. Reference: Hamid et al.[34] 2024.

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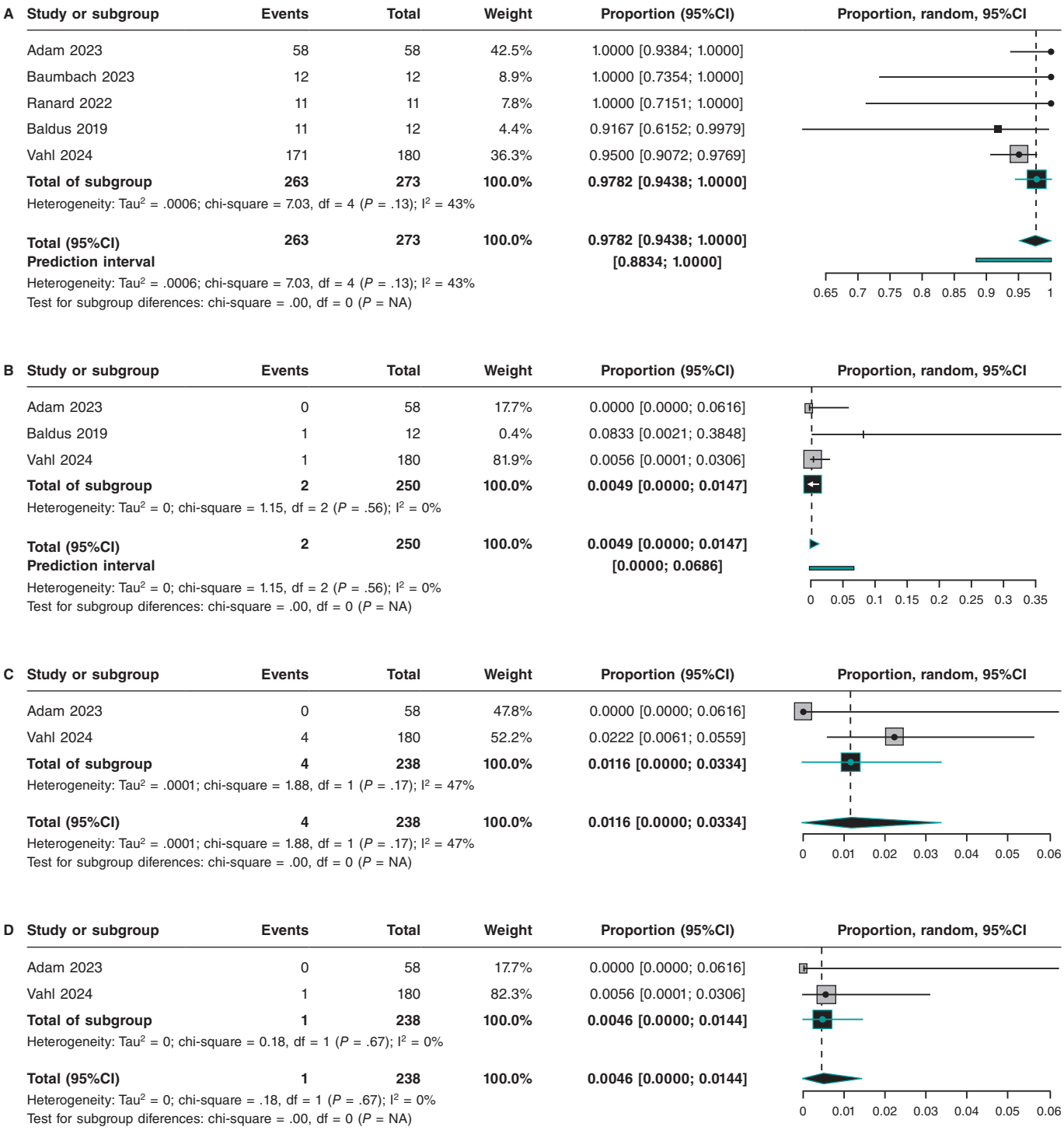

Figure 2. A. Forest plot of procedural success of TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baumbach et al.[26] 2023, Ranard et al.[27] 2022, Baldus et al.[28] 2019, Vahl et al.[32] 2024; B. Forest plot of conversion to surgery TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baldus et al.[28] 2019, Vahl et al.[32] 2024; C. Forest plot of device migration/embolization TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Vahl et al.[32] 2024; D. Forest plot of need for a second valve TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Vahl et al.[32] 2024. 95%CI, 95% confidence interval.

aortopathy, no cases of annular rupture were reported with the 2 self-expanding dedicated devices. We also observed low rates of acute kidney injury, bleeding, vascular complications, and in-hospital mortality. Whether this low rate of early complications will translate into improved long-term clinical outcomes remains to be determined and should be explored in longitudinal prospective studies.

A major challenge associated with TAVI for native pure/predominant AR is the risk of device migration/embolization and paravalvular leakage. This risk arises from the absence of calcification in the landing zone, the large size of the aortic annulus, and the high stroke volume in AR patients. The design of the 2 AR-dedicated TAVI devices aims is to mitigate this risk (figure 5).

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Table 6. Quantitative analysis of in-hospital outcomes of transfemoral transcatheter aortic valve implantation for aortic regurgitation

Variables	Reporting studies (n)	Total patients (n)	Proportion with the endpoint (95%CI)	Heterogeneity
Procedural success	5	273	0.9782 (0.9438-1.000)	I^2 = 43%, *P* = .13
Device success	2	228	0.9704 (0.9484-0.9924)	I^2 = 0%, *P* = .61
Conversion to surgery	3	250	0.0049 (0.0000-0.0147)	I^2 = 0%, *P* = .56
Device migration/ embolization	2	238	0.0116 (0.0000-0.0334)	I^2 = 47%, *P* = .17
Need for a second Valve	2	238	0.0046 (0.0000-0.0144)	I^2 = 0%, *P* = .67
Bleeding, major or life-threatening	3	250	0.0249 (0.0000-0.0656)	I^2 = 66%, *P* = .05
Vascular complications	4	262	0.0572 (0.0174-0.0969)	I^2 = 61%, *P* = .05
Acute kidney injury	3	250	0.0592 (0.000-0.1386)	I2 = 72%, *P* = .03
In-hospital mortality	3	250	0.0000 (0.0000-0.0073)	I^2 = 0%, *P* = 1.00

95%CI, 95% confidence interval.

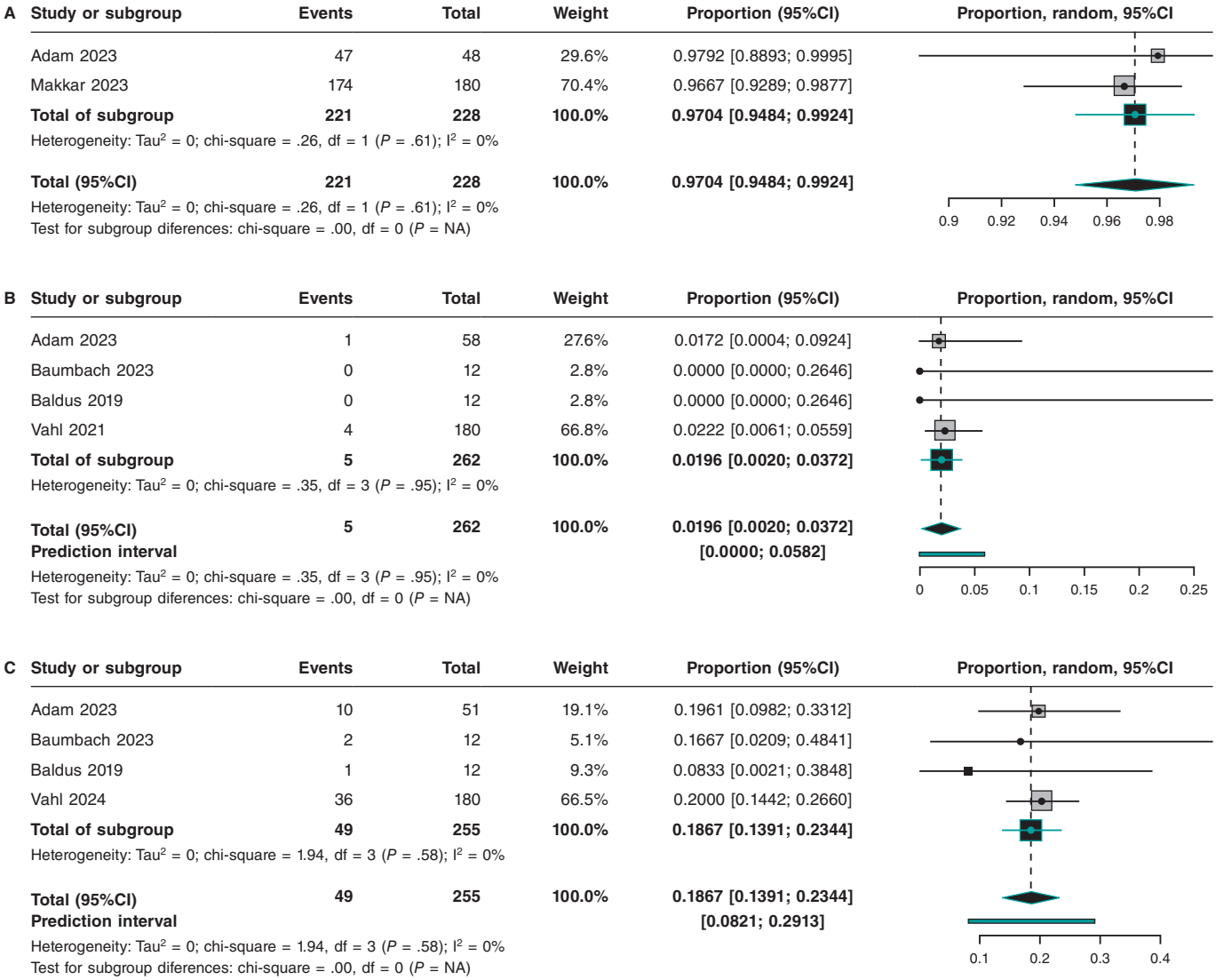

Figure 3. A. Forest plot of device success TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Makkar et al.[33] 2023; B. Forest plot of 30-day all-cause mortality TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baumbach et al.[26] 2023, Baldus et al.[28] 2019, Vahl et al.[32] 2024; C. Forest plot of 30-day permanent pacemaker implantation TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baumbach et al.[26] 2023, Baldus et al.[28] 2019, Vahl et al.[32] 2024.

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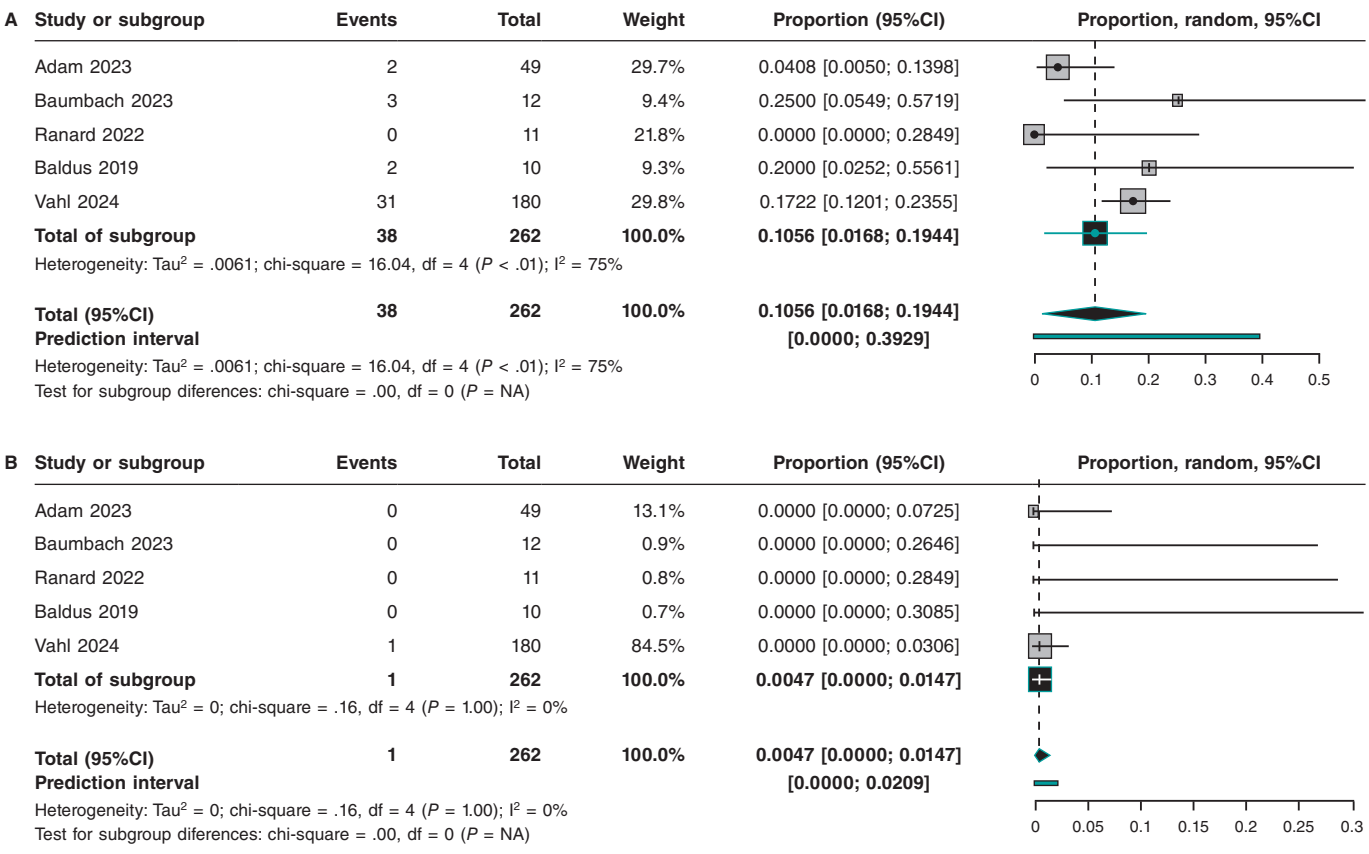

Figure 4. A. Forest plot of 30-day of mild prosthetic valve regurgitation TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baumbach et al.[26] 2023, Ranard et al.[27] 2022, Baldus et al.[28] 2019, Vahl et al.[32] 2024; B. Forest plot of 30-day of greater than mild prosthetic valve regurgitation TF JenaValve. The bibliographical references mentioned in this figure correspond to: Adam et al.[25] 2023, Baumbach et al.[26] 2023, Ranard et al.[27] 2022, Baldus et al.[28] 2019, Vahl et al.[32] 2024.

Table 7. Quantitative analysis of 30-day outcomes of transfemoral transcatheter aortic valve implantation for aortic regurgitation

Variables	Reporting studies (n)	Total patients (n)	Proportion with the endpoint (95%CI)	Heterogeneity
30-day all-cause mortality	4	262	0.0196 (0.0020-0.0372)	I^2 = 0%, P = .95
30-day stroke	3	250	0.0112 (0.0000-0.0316)	I^2= 0%, P = .38
30-day PPM implantation	4	255	0.1867 (0.1391-0.2344)	I^2 = 0%, P = .58
30-day mild PVR	5	262	0.1056 (0.0168-0.1944)	I^2 = 75%, P < .01
30-day moderate PVR	5	262	0.0047 (0.0000-0.0147)	I^2 = 0%, P = 1.00

95%CI, 95% confidence interval; PPM, permanent pacemaker; PVR, prosthetic valve regurgitation.

The JenaValve device features an natomically-oriented design with 'supporting arms' that can be positioned in the sinuses of the aortic root, ensuring precise placement of the valve stent. Additionally, the fixation of the oriented device to the native valve leaflet through clip attachment provides an extra axial expansion force, enabling secure fixation even in the absence of leaflet calcifications.[37]

The J-Valve device is characterized by its U-shaped grasper that captures the aortic valve leaflets, achieving 'axial' fixation, which complements the 'radial' fixation, which is less reliable in the absence of calcification. Furthermore, the dual-phase release mechanism of this device (the graspers are initially released, followed by the valve) can aid in precise placement of the graspers prior to valve deployment and decrease the likelihood of damage to the native valve.[38]

Our data suggest that these innovative designs are associated with very low rates of device dislocation and paravalvular leakage, which in turn results in low rates of second valve requirement and surgical conversion. Importantly, these benefits did not come at the expense of increased risk of annular injury or coronary obstruction. However, a relatively high rate of PPI was observed with JenaValve, reaching nearly 19% in 5 studies of its updated transfemoral version. This may reflect a tendency for a relatively deeper implantation, a common issue with early experience of nearly all TAVI systems that tends to improve over time and typically portends a decline in PPI rates.[39-42]

While the current review includes preliminary single-arm, observational, small-scale studies, several randomized trials are have been conducted on J-Valve and JenaValve.[43-47] While the results of these trials are pending, our data suggest a positive outcome.

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TAVI systems designed for pure AR

Common features:
- Supra-annular, trileaflet bioprosthesis
- Self-expanding nitinol frame with large, open cell design
- Self-aligning technology

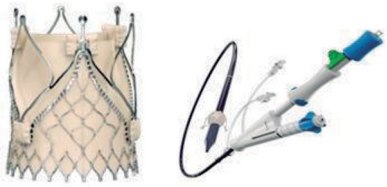
	J-Valve	JenaValve Trilogy
		
Bioprosthesis	Bovine pericardial tissue	Porcine pericardial tissue
TF delivery system	18,21 Fr	18 Fr
Aligning/anchoring	3 anchor rings	3 locators
Size matrix	5 sizes (22-25-28-31-34 mm)	3 sizes (S, M, and L)
Annulus size range	Diameter: 18-33 mm Perimeter: 57-104	Diameter: 21-27 mm Perimeter: 67 to 85 mm
Frame height	17-25 mm	31.3-35.7 mm

Figure 5. Central illustration. Features of the contemporary generations of 2 TAVI systems dedicated to aortic regurgitation.

In the currently available data, there is a dominance of transapical access procedures among J-Valve implantations. However, with the trend toward more minimalistic TAVI procedures, the transapical approach may only be a precursor, with the transfemoral approach expected to eventually become the standard, as already observed with the JenaValve. The most recent data, presented in 2023, on transfemoral J-Valve procedures (from the compassionate use experience in North America) is particularly reassuring.[20]

Study limitations

The scope of our investigation was restricted to observational studies, abstracts, and conference presentations;, none of which were randomized controlled trials. This inherently limits the quality of the evidence produced. Additionally, the present findings may have been influenced by publication bias favoring TAVI for native pure or predominant AR, which was mitigated by our. However, we sought to mitigate this bias through an exhaustive review of the available literature and the meticulous exclusion of overlapping or duplicate data. The total patient population remained relatively small, and follow-up was restricted to 30-day outcomes, so the findings should be interpreted with these limitations in mind.

CONCLUSIONS

This systematic review provides a comprehensive and up-to-date analysis of data on TAVI with dedicated devices for native pure/predominant AR. The initial experience discussed in the present review demonstrates the safety and favorable early outcomes of TAVI using J-Valve and JenaValve in patients with pure/predominant AR, especially when the transfemoral approach is used. Nevertheless, PPI requirement remains frequent.

FUNDING

None.

ETHICAL CONSIDERATIONS

The present article is a literature review and, as such, ethics approval was not required. The study did not involve patient recruitment or access to disaggregated information on individuals and therefore informed consent was not required. Possible sex/gender biases have been taken into account in the preparation of this article.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this article.

AUTHORS' CONTRIBUTIONS

A. Hassan, M. Abdelshafy, and R.A. Diab performed the literature review, data analysis, and initial manuscript drafting. H. Wienemann, M. Adam, S. García, and M. Saad critically reviewed the manuscript. M. Abdelghani conceived the idea, designed and supervised data collection and analysis, and finalized the manuscript.

CONFLICTS OF INTEREST

M. Adam reports personal fees and speaker honoraria from Abbott, Boston Scientific, Edwards Lifesciences, JenaValve, and Medtronic. S. Garcia reports institutional grants from J.C. Medical and JenaValve. All other authors have no conflict of interest to report.

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WHAT IS KNOWN ABOUT THE TOPIC?

– The off-label use of the next-generation nondedicated TAVI devices to treat pure AR is associated with an increased risk of device embolization and PVR.

WHAT DOES THIS STUDY ADD?

– TAVI for AR with devices specifically designed for this indication (J-Valve and JenaValve) shows favorable early safety and efficacy, especially when the transfemoral approach is used. Nevertheless, the need for PPI remains frequent.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M24000477.

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