Comparison of Long-term Efficacy of Domestic TAVR vs. Corevalve

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Abstract: Aim: To assess the long-term effects of domestic valves and compare them with similar products to demonstrate non-inferiority and provide guidance for valve selection in severe aortic stenosis patients. Methods: The study comprised two parts: evaluating the long-term effects of domestic valves through follow-up data, and conducting a meta-analysis to assess the long-term efficacy of Corevalve. Results: Both valves showed high cumulative all-cause mortality and cardiac mortality rates at 5 years post-surgery, with statistically significant differences. There were also significant differences in the cumulative incidence rates of new pacemaker implantation and cardiac rehospitalization. Stroke and myocardial infarction event rates within 5 years were both below 10%, with no statistically significant differences. Conclusion: Domestic valves demonstrated favorable long-term effects, performing comparably or even superior to Corevalve in certain aspects.
***Keywords*:** aortic stenosis; transcatheter aortic valve replacement; TAVR

1. Introduction

Aortic stenosis (AS) is a common valvular disease, with untreated severe symptomatic AS often resulting in mortality. Preferred treatments include Transcatheter Aortic Valve Replacement (TAVR) and Surgical Aortic Valve Replacement (SAVR). Since the first successful TAVR, subsequent studies have shown favorable outcomes. TAVR provides a viable option for patients unsuitable for SAVR and has become the primary treatment for elderly AS patients. In China, TAVR development started relatively late, with Academician Dr. Ge performing the first domestic TAVR in October 2010 [2], marking the country's initiation of TAVR. Despite advancements in China's implantable medical device industry, there remains a gap compared to foreign counterparts. Although some clinical comparisons between domestic and imported valves have been conducted [1], the research period is short, and information on long-term efficacy comparisons is limited, necessitating further investigation. Current valve guidelines emphasize considering postoperative relative risks and long-term outcomes, highlighting the crucial importance of postoperative long-term clinical effects for all TAVR valves. Therefore, this article aims to compare the long-term efficacy of domestic and imported TAVR valves, explore the non-inferiority of domestic products, and evaluate their long-term effects, providing guidance for valve selection in patients with severe AS.

2. Methods

The study comprised two parts: a long-term follow-up of the domestic valve and a meta-analysis of the comparable Corevalve. The 5-year postoperative data of the domestic product were obtained from a prolonged investigation within a prospective, multicenter, single-arm clinical trial conducted from September 2012 to June 2014. This trial enrolled cases implanted with a specific domestic TAVR valve and followed them for 5 years postoperatively. The primary endpoint was all-cause mortality or severe stroke, while secondary endpoints included MACCE events, stroke events, and the rate of cardiac rehospitalization. Statistical analysis was performed using Minitab software. Continuous variables were expressed as mean ± standard deviation for normally distributed data, and frequency and composition ratio were utilized for count data. Two-sided tests were employed for comparisons, with a p-value <0.05 considered statistically significant.

Simultaneously, computer searches were conducted in Embase, PubMed, Web of Science, Cochrane Library, Clinical Trials.com, CNKI, Wanfang Data, VIP, and China Clinical Trial Center, covering the period from database establishment to October 2023. Chinese search terms included transcatheter aortic valve replacement, Aortic stenosis, Medtronic, etc., while English terms encompassed TAVR, Corevalve, Evolut, Aortic stenosis, Medtronic, etc. Language was limited to English and Chinese, and keywords were restricted to Human, English, and Clinical trial. Inclusion criteria comprised subjects diagnosed with AS unsuitable for conventional surgical treatment, studies evaluating the long-term efficacy of the Corevalve, and each study describing at least one outcome indicator: all-cause mortality or severe stroke at 5 years post-TAVR, incidence of MACCE events, stroke events, and heart failure rehospitalization. Exclusion criteria included case reports, conference reports, reviews, etc., as well as literature with incomplete data extraction or obvious errors. Duplicate literature was managed via EndNote, followed by screening out irrelevant studies based on titles and abstracts. Full-text review was conducted to determine inclusion. StataMP 14 facilitated meta-analysis, and heterogeneity was assessed using the I^2 statistic. Sensitivity analysis was performed to assess result stability, and funnel plots and symmetry tests were employed to detect publication bias.

3. Outcomes

The first part: In the first part, a total of 101 subjects were initially included for the domestic product, with 86 subjects enrolled in the extended study 2-5 years post-procedure. The average age was 75.86 years, with 57.4% being male. Baseline characteristics revealed that 20.8% had a history of syncope, 16.8% had diabetes, 31.7% had hyperlipidemia, 16.8% had a smoking history, 49.5% had hypertension, 48.5% had heart failure, 14.9% had atrial fibrillation, and 14.9% had a history of cerebrovascular disease. Among the 86 subjects in the extended study, one was lost to follow-up after 4 years, leaving data available for 85 subjects at 5 years post-TAVR. By December 2020, 29 subjects had died during follow-up, resulting in a cumulative all-cause mortality incidence rate of 34.1% at 5 years post-TAVR with the domestic valve. Among them, 9 experienced cardiac-related deaths, with a cumulative incidence rate of 10.6%. The cumulative incidence rate of stroke events during follow-up was 5.9%. Additionally, the cumulative incidence rates were 37.6% for MACCE events, 3.5% for myocardial infarction （MI）events, 3.5% for renal insufficiency events, 24.7% for new pacemaker implantation (PPI), and 15.25% for cardiac rehospitalization.

The second part: A total of 2395 articles were retrieved from the database search. After excluding 479 duplicate articles and 307 articles, such as reviews, systematic reviews, comments, and case reports, further screening of titles and abstracts led to the exclusion of 1562 articles due to irrelevant content or inconsistent intervention measures. Upon full-text review, 39 articles with inconsistent endpoint data were excluded. Following a hierarchical selection process based on inclusion criteria, 8 articles, involving 3068 patients, were ultimately included for analysis. The included studies achieved a MINORS quality assessment score of ≥12 points, indicating high quality. The basic characteristics of the included studies are presented in Table 1.

(1) Summary of Meta-Analysis Results: The heterogeneity test results for the cumulative overall mortality, cardiovascular mortality, stroke incidence, cardiac rehospitalization rate, and new PPI rate showed $P < 0.1$, $I^2 > 50\%$, hence a random-effects model was used. The heterogeneity test result for the MI rate showed $P > 0.1$, $I^2 < 50\%$, and therefore a fixed-effects model was used. The summary effect size results are shown in Table 2. Meta-regression found that publication time, patient age, STS score, gender, history of PCI, and NYHA classification were unrelated to study heterogeneity, and further consideration of other factors is needed in the future to address the source of heterogeneity.

(2) Sensitivity Analysis Results: Sensitivity analysis was performed for each event result, and it was found that no single article significantly influenced the results, indicating stability.

(3) Publication Bias Assessment: A funnel plot symmetry test was conducted for each event, showing that the scatter plots were generally symmetrical on both sides and mostly within the 95% confidence interval, indicating no apparent publication bias. Additionally, Begg's Test and Egger's Test yielded $p > 0.05$, suggesting funnel plot symmetry, indicating no publication bias in this study's literature..

Table 1. Basic Characteristics of Included Studies

Literature	cases	Age (years)	Male, % (n)	Smoking History (%)	BMI (kg/m²)	STS Score (%)	NYHA Classification III–IV, % (n)
Marco 2015[3]	353	81.5±6.3	44.5 (157)	NS	NS	9.5±10.0	70 (247)
Pablo 2017[4]	108	78.6 ± 6.7	45.4 (49)	16.7 (18/108)	28.0±5.2	NS	58.4 (63)
Ulrich 2017[5]	996	81.1±6.4	49.3 (491)	32.4 (323/996)	NS	6.4 ± 4.4	80.0 (783)
Thomas 2018[6]	391	83.2 ± 7.1	47.1 (184)	NS	NS	7.3 ± 3.0	85.4 (334)
Erik 2018[7]	152	81**	47.3 (72)	NS	NS	4.4**	93.4 (142)
René 2019[8]	309	82.8±5.1	53.7 (166)	NS	25.9±4.8	6.9 ± 4.8	67.6 (208)
Mohamed 2020[9]	120	79.6±15.8	28.3 (34)	NS	26.5±5.2	6.2±3.9	81.7 (98)
Suzanne 2021[10]	639	82.8±8.4	47 .4 (303)	NS	NS	10.4±5.6	91.9 (587)

Comparison: In this study, both the long-term follow-up data of domestic TAVR valve and the meta-analysis data of Corevalve group showed significantly high 5-year cumulative all-cause mortality and cardiovascular mortality rates (all-cause mortality: 34.1% vs 49%, P=0.002＜0.05; cardiovascular mortality: 10.6% vs 27%, P=0.000＜0.05). For other complications, such as the cumulative incidence rate of new PPI and cardiac rehospitalization, significant differences were observed between the two methods (cumulative incidence rate of new PPI: 24.7% vs 35%, P=0.000＜0.05; cardiac rehospitalization rate: 15.25% vs 33%, P=0.000＜0.05). Additionally, the 5-year cumulative incidence rate of MACCE events with domestic TAVR valve was 37.6%, including death, stroke, myocardial infarction, and renal failure. The rates of these composite events was not reported in the meta-analysis literature of Corevalve group, but the rates of stroke and MI events at 5 years were reported. Both groups had a low rates of stroke and MI events at 5 years, and the differences were not statistically significant (stroke rate: 5.9% vs 10%, P= 0.126＞0.05; MI rate: 3.5% vs 3%, P= 0.729＞0.05).

Table 1 (continued). Basic Characteristics of Included Studies（Medical History）

Literature	Atrial Fibrillation , % (n)	Hypertension, % (n)	Hypercholesterolemia , % (n)	Diabetes, % (n)	Cerebrovascular Disease , % (n)	Myocardial Infarction , % (n)	PCI , % (n)	CABG, % (n)	BAV , % (n)
Marco 2015[3]	1.4 (5)	75.6 (267)	NS	30.3 (107)	NS	7.4 (26)	30.0 (106)	15.3 (54)	NS
Pablo 2017[4]	NS	65.7 (71)	50.9 (55)	23.1 (25)	NS	NS	13.9 (15)	NS	NS
Ulrich 2017[5]	33.5 (331)	78.8 (782)	53.9 (528)	31.3 (308)	13.4 (131)	NS	31.4 (310)	21.3 (211)	NS
Thomas 2018[6]	40.9 (160)	NS	NS	34.8 (136)	25.1 (97)	NS	34.3 (134)	29.4 (115)	NS
Erik 2018[7]	NS	82.2(125)	NS	26.3 (40)	NS	22.4 (32)	60.0 (91)	21.1 (32)	NS
René 2019[8]	32.4 (100)	83.8 (259)	60.5 (187)	25.2 (78)	NS	NS	26.5 (82)	5.5 (17)	NS
Mohamed 2020[9]	24.8 (29)	NS	NS	NS	NS	NS	42.5 (51)	12.5 (15)	NS
Suzanne 2021[10]	NS	NS	NS	39.7 (254)	NS	NS	35.8 (229)	39.7 (254)	21.0 (134)

**Median

Table 2. Summary of Meta-Analysis Results

Events	Included Studies	Statistical Type	Heterogeneity		Summary Effect Size	95% CI	Z Value	P Value
			p	I^2, %				
All-cause mortality rate	7 Studies [3-9]	Random-effects model	0.06	50.66	0.49	[0.46, 0.52]	46.64	0.00
Cardiac mortality rate	7 Studies [3-9]	Random-effects model	0.00	80.61	0.27	[0.23, 0.32]	20.53	0.00
Myocardial infarction incidence rate	5 Studies [5,6,8-10]	Fixed-effects model	0.43	0.00	0.03	[0.02, 0.04]	14.84	0.00
Stroke incidence rate	6 Studies [3,5,6,8-10]	Random-effects model	0.00	84.96	0.10	[0.08, 0.14]	11.73	0.00
Cardiac rehospitalization rate	4 Studies [3,6,9,10]	Random-effects model	0.00	90.95	0.33	[0.25, 0.42]	9.42	0.00
New PPI rate	5 Studies [3,5,6,9,10]	Random-effects model	0.06	55.19	0.35	[0.32, 0.39]	34.7	0.00

4. Discussion

While TAVR's short and mid-term benefits are well-established globally, long-term data on TAVR valve durability, especially for domestic versions, are lacking, with few 5-year outcome reports. Our study aims to address this gap by presenting detailed 5-year event rates of a specific domestic TAVR valve, providing insights into its long-term performance. Additionally, we conducted a meta-analysis of eight high-quality Corevalve studies (n=3068) to ensure a robust evaluation. By comparing outcomes with Corevalve, we aimed to assess the non-inferiority of domestic TAVRs, thereby supporting their substitution for imported devices. Key studies such as REPRISE III, SURTAVI, and PARTNER 3 have further bolstered the clinical utility of TAVR by demonstrating equivalent 5-year outcomes for TAVR and surgery across various risk groups.

However, it's important to acknowledge the limitations of our study, including a small sample size, specific patient population, unclear baseline data in some literature, and a lack of global representation in the meta-analysis. Future research efforts should focus on addressing these gaps to strengthen the evidence base for domestic TAVR valves..

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