ORIGINAL RESEARCH

Valve-in-Valve for Degenerated Transcatheter Aortic Valve Replacement Versus Valve-in-Valve for Degenerated Surgical Aortic Bioprostheses: A 3-Center Comparison of Hemodynamic and 1-Year Outcome

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BACKGROUND: As transcatheter aortic valve replacement (TAVR) is expected to progress into younger patient populations, valve-in-TAVR (ViTAVR) may become a frequent consideration. Data on ViTAVR, however, are limited. This study investigated the outcome of ViTAVR in comparison to valve in surgical aortic valve replacement (ViSAVR), because ViSAVR is an established procedure for higher-risk patients requiring repeated aortic valve intervention.

METHODS AND RESULTS: Clinical and procedural data of patients who underwent ViTAVR at 3 sites in the United States and Germany were retrospectively compared with data of patients who underwent ViSAVR at Cedars-Sinai Medical Center, according to Valve Academic Research Consortium-2 criteria. A total of 99 consecutive patients, 52.5% women, with a median Society of Thoracic Surgeons score of 7.2 were identified. Seventy-four patients (74.7%) underwent ViSAVR, and 25 patients (25.3%) underwent ViTAVR. Balloon-expandable devices were used in 72.7%. ViSAVR patients presented with smaller index devices (21.0 versus 26.0 mm median true internal diameter; $P<0.001$). Significantly better postprocedural hemodynamics (median prosthesis mean gradient, 12.5 [interquartile range, 8.8–16.2] versus 16.0 [interquartile range, 13.0–20.5] mm Hg; $P=0.045$) were observed for ViTAVR compared with the ViSAVR. Device success, however, was not different (79.2% and 66.2% for ViTAVR and ViSAVR, respectively; $P=0.35$), as were rates of permanent pacemaker implantation (16.7% versus 5.4%; $P=0.1$). One-year-mortality was 9.4% and 13.4% for ViTAVR and ViSAVR, respectively (log-rank $P=0.38$).

CONCLUSIONS: Compared with ViSAVR, ViTAVR provides acceptable outcomes, with slightly better hemodynamics, similar device success rates, and similar 1-year mortality.

Key Words: aortic surgery ■ aortic valve replacement ■ structural valve deteriotation ■ transcutaneous aortic valve implantation ■ valve-in-valve

solated redo surgery for degenerated surgical bioprosthetic aortic valves (AV) accounts for ≈6.9% of all AV procedures.[1] Redo surgery in intermediate-risk patients can be performed with acceptable clinical outcomes. Compared with primary surgical aortic valve replacement (SAVR), however, redo SAVR is

CLINICAL PERSPECTIVE

What Is New?

- This is the first study comparing valve in transcatheter aortic valve replacement (TAVR) with valve in surgical aortic valve replacement.
- Although valve-in-TAVR seems to result in slightly superior hemodynamics, rates of residual gradients >19 mm Hg, and thus device success, as well as 1-year mortality do not differ compared with valve in surgical aortic valve replacement.

What Are the Clinical Implications?

- Considering the increasing number of patients treated using TAVR, valve-in-TAVR may potentially serve as a valuable treatment option for degenerated TAVR devices.
- In vitro experiments that address hemodynamic aspects of valve-in-TAVR should be promoted.

Nonstandard Abbreviations and Acronyms

AR	aortic regurgitation
AV	aortic valve
PVL	paravalvular leakage
SAVR	surgical aortic valve replacement
TAVR	transcatheter aortic valve replacement
ViSAVR	valve-in-SAVR
ViTAVR	valve-in-TAVR
ViV	valve-in-valve

associated with increased 30-day mortality, postoperative stroke, and pacemaker implantation.[2] Because of increased age and risk profile, as well as adhesions related to the previous procedure, redo SAVR patients are generally at higher surgical risk and may therefore be denied for repeated intervention. Following conceptualization using an animal model in 2007, transcatheter valve-in-valve (ViV) for failed surgical bioprosthetic AVs (valve-in-SAVR [ViSAVR]) has gained attention as a therapeutic option for patients at high or prohibitive surgical risk.[3] ViSAVR is considered safe, effective, and reproducible.[4–7]

Bioprostheses are prone to structural valve degeneration, resulting in limited long-term durability.[8] Although yet unproved, similar processes are also likely to occur in transcatheter aortic valve replacement (TAVR) prostheses. As TAVR has proved to provide at least similar clinical outcomes compared with SAVR for a range of patients, including younger and lower-risk populations, structural valve degeneration will also be more frequently observed in TAVR

patients.[9,10] As infective endocarditis following TAVR is rare (incidences of 1.1%–1.8% per patient-year),[11,12] valve-in-TAVR (ViTAVR) might become a frequent consideration for failed TAVR devices. However, limited data exist for TAVR as ViV for patients with degenerated TAVR valves.[13] Furthermore, to the best of our knowledge, no data exist to compare ViTAVR against ViSAVR with regard to clinical and hemodynamic outcome.

METHODS

The analytical methods used in this study are available from the first author on request.

Study Population

For this study, baseline, procedural, and clinical data of patients who underwent repeated intervention for degenerated TAVR or SAVR between November 4, 2009, and May 10, 2018, were retrospectively collected. Data on ViTAVR were collected at 3 sites in the United States and Germany (Cedars-Sinai Medical Center, Los Angeles, CA; Heart Center Leipzig, Leipzig, Germany; and Heart Center Dresden, Dresden, Germany). Within this study period, n=15 patients underwent ViTAVR for paravalvular leakage (PVL). These patients are excluded from this analysis. For the ViSAVR group, data of 2 widely used SAVR devices were retrospectively collected for consecutive patients at Cedars-Sinai Medical Center (Carpentier Edwards Perimount, Edwards Lifesciences, CA: n=56 [75.7%]; and Medtronic Mosaic, Medtronic, Minneapolis, MN: n=18 [24.3%]).

Devices

In the ViTAVR group, valve models at index procedure included the following: CoreValve (Medtronic; n=5 [20%]); Sapien XT (Edwards Lifesciences Corp, Irvine, CA; n=6 [24%]); Sapien (n=10 [40%]); Acurate neo (Boston Scientific, Marlborough, MA; n=1 [4%]); Sapien 3 (Edwards Lifesciences; n=1); JenaValve (JenaValve Technology GmbH, Munich, Germany; n=1); and Ventor (Medtronic; n=1).

Indication for ViV was categorized on the basis of the mode of prosthesis dysfunction, as follows: (1) aortic stenosis: mean prosthesis gradient >19 mm Hg, aortic regurgitation (AR) < moderate, and PVL < moderate; (2) AR: transvalvular AR > mild, mean prosthesis gradient <20 mm Hg, PVL < moderate; (3) PVL > mild; (4) combined: mean prosthesis gradient >19 mm Hg, AR > mild. Prosthesis stenosis was defined as being severe for mean prosthesis gradient >40 mm Hg.

Valve sizes were defined on the basis of true internal diameter.[14]

End Point Definitions

The primary outcome was all-cause 1-year mortality, and the composite end points of device success and early safety were based on the Valve Academic Research Consortium-2 criteria.[15] The study hypothesis was that ViTAVR is superior to ViSAVR in terms of the primary outcome. Device success was defined as follows: (1) absence of procedural mortality; (2) correct valve positioning without requirement for second ViV; and (3) adequate prosthesis performance on the basis of mean postprocedural gradient <20 mm Hg and grade of prosthetic regurgitation < moderate. Early safety at 30 days was assessed using all-cause mortality, stroke (disabling and nondisabling), life-threatening bleeding, acute kidney injury (stage 2 or 3; including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeated procedure. Conduction disturbances and arrhythmia were summarized using a combined end point of new arrhythmia based on Valve Academic Research Consortium-2 criteria or new permanent pacemaker implantation within 30 days. Hemodynamic outcome was assessed at 1 and 30 days and was 96% and 66.7% complete, respectively. Retrospective data collection was approved by the ethic committees of the respective sites, and need for individual patient consent was waived.

Statistical Analysis

Normality of data was evaluated using Shapiro-Wilk tests. Continuous variables of normal distribution were compared using Student t test and are shown as mean±SD. Continuous variables without normal distribution were compared using Wilcoxon rank-sum or Kruskal-Wallis test and are shown as median±interquartile range (IQR). Categorical variables were compared using χ^2 or exact Fisher test (for expected frequencies <5) and are shown as frequencies and percentages. Survival curves were analyzed and presented using the Kaplan-Meier algorithm. Difference between survival was analyzed using log-rank test. Data analysis followed recommendations of reproducible research using RStudio version 1.1.453 (RStudio Team [2016]; RStudio: Integrated Development for R; RStudio, Inc, Boston, MA; http://www.rstudio.com/).[16] The following packages were included: *compareGroups, DiagrammeR, dplyr, ggplot2, gridExtra, lubridate, survival,* and *rmarkdown.*[17]

RESULTS

Baseline Characteristics
Study Population

During this study period, a total of 8541 patients underwent native TAVR at the 3 centers. A total of 100 ViV patients were identified for this study; 99 patients (52 [52.5%] women) with a median Society of Thoracic Surgeons score of 7.2% (IQR, 4.3%–13.4%) were included. One ViTAVR patient was excluded because of early ViTAVR 3 days following the index procedure. Of 99 ViV patients, 74 (74.7%) underwent ViSAVR and 25 (25.3%) underwent ViTAVR (Figure 1).

ViTAVR patients were, on average, 6 years older (P=0.058) and presented with higher rates of chronic obstructive lung disease (P=0.006; Table 1). Seventeen patients (14.9%) presented with small (ie, true internal valve diameter <19 mm) index devices, all of which were in the ViSAVR group (23% of all valves in the ViSAVR group). Coronary artery disease and prior coronary interventions were common in both groups (combined frequency of percutaneous coronary intervention and
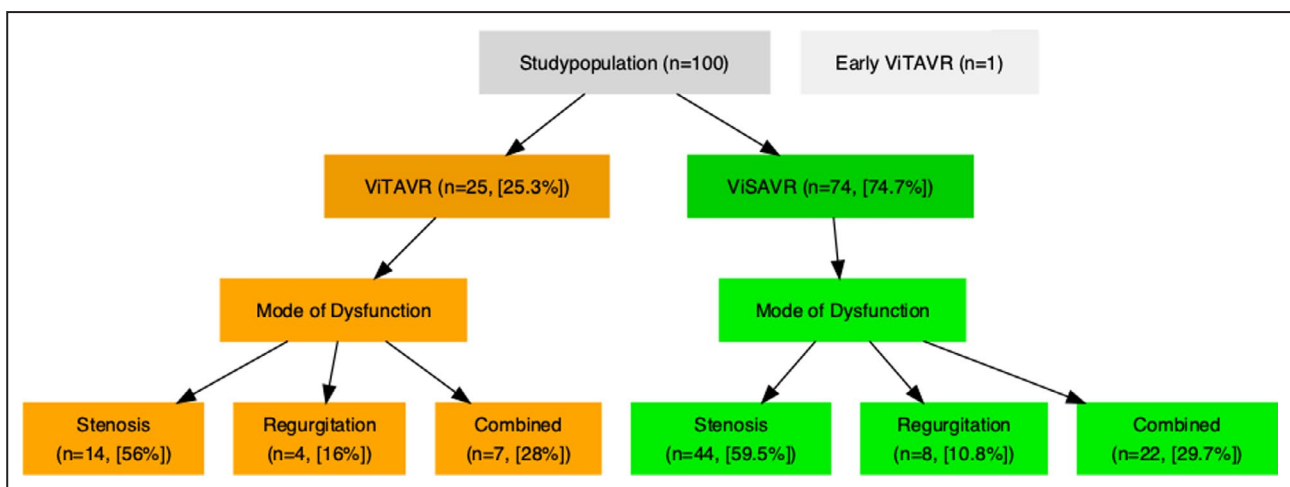

Figure 1.   Study population.
Ninety-nine individuals were included to compare hemodynamic and clinical outcome of valve in transcatheter aortic valve replacement (ViTAVR; orange) against valve in surgical aortic valve replacement (ViSAVR; green).

Table 1.   Baseline Characteristics of the Study Population

Characteristic	All (N=99)	ViTAVR (N=25)	ViSAVR (N=74)	P Value (Overall)
Age, y	80.0 (73.0–86.0)	83.0 (80.0–86.0)	77.0 (69.2–86.0)	0.058
Women				0.526
No	47 (47.5)	10 (40.0)	37 (50.0)	
Yes	52 (52.5)	15 (60.0)	37 (50.0)	
STS score	7.15 (4.31–13.4)	7.44 (5.65–14.2)	6.80 (3.74–12.3)	0.066
NYHA functional class				0.328
II	3 (3.06)	1 (4.00)	2 (2.74)	
III	48 (49.0)	15 (60.0)	33 (45.2)	
IV	47 (48.0)	9 (36.0)	38 (52.1)	
CCS class				0.118
0	78 (80.4)	18 (72.0)	60 (83.3)	
I	7 (7.22)	1 (4.00)	6 (8.33)	
II	8 (8.25)	3 (12.0)	5 (6.94)	
III	3 (3.09)	2 (8.00)	1 (1.39)	
IV	1 (1.03)	1 (4.00)	0 (0.00)	
Diabetes mellitus				0.115
No	69 (70.4)	14 (56.0)	55 (75.3)	
Yes	29 (29.6)	11 (44.0)	18 (24.7)	
Chronic obstructive lung disease				0.006
No	64 (64.6)	10 (40.0)	54 (73.0)	
Yes	35 (35.4)	15 (60.0)	20 (27.0)	
Creatinine clearance <60, ml/min				0.920
No	42 (42.9)	10 (40.0)	32 (43.8)	
Yes	56 (57.1)	15 (60.0)	41 (56.2)	
Previous coronary artery bypass surgery				0.319
No	61 (61.6)	18 (72.0)	43 (58.1)	
Yes	38 (38.4)	7 (28.0)	31 (41.9)	
Previous PCI				0.304
No	86 (86.9)	20 (80.0)	66 (89.2)	
Yes	13 (13.1)	5 (20.0)	8 (10.8)	
Previous TIA or stroke				1.000
No	77 (77.8)	19 (76.0)	58 (78.4)	
Yes	22 (22.2)	6 (24.0)	16 (21.6)	
Permanent aFib				0.580
No	62 (62.6)	14 (56.0)	48 (64.9)	
Yes	37 (37.4)	11 (44.0)	26 (35.1)	
Permanent pacemaker or defibrillator				1.000
No	77 (79.4)	20 (80.0)	57 (79.2)	
Yes	20 (20.6)	5 (20.0)	15 (20.8)	
Ejection fraction, %	60.0 (45.0–65.5)	59.0 (55.0–69.0)	60.0 (44.0–65.0)	0.354
AV mean gradient, mm Hg	40.0 (26.0–49.5)	40.0 (24.0–62.0)	40.0 (26.2–47.8)	0.939
AV peak gradient, mm Hg	64.0 (45.2–84.8)	63.0 (46.0–105)	66.0 (45.0–84.0)	0.938
AR > mild				0.797
No	57 (58.2)	15 (62.5)	42 (56.8)	
Yes	41 (41.8)	9 (37.5)	32 (43.2)	
MR > mild				0.354
No	61 (62.2)	18 (72.0)	43 (58.9)	
Yes	37 (37.8)	7 (28.0)	30 (41.1)	

(Continued)

Table 1.   Continued

Characteristic	All (N=99)	ViTAVR (N=25)	ViSAVR (N=74)	P Value (Overall)
Index AVR <19.0 mm true ID				0.005
No	82 (82.8)	25 (100)	57 (77.0)	
Yes	17 (17.2)	0 (0.00)	17 (23.0)	

Values are shown as median (interquartile range) for continuous variables and number (percentage) for categorical variables. Group differences are presented as overall P value. aFib indicates atrial fibrillation; AR, aortic regurgitation; AV, aortic valve; AVR, AV replacement; CCS, Canadian Cardiovascular Society; ID, internal diameter; MR, mitral regurgitation; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; TIA, transient ischemic attack; ViSAVR, valve in surgical AVR; and ViTAVR, valve in transcatheter AVR.

coronary artery bypass surgery in ViTAVR and ViSAVR of 48% and 52.7%, respectively).

For ViTAVR, 88% of the index devices were either balloon-expandable Sapien (77.3%; n=17) or self-expanding CoreValve prostheses (22.7%; n=5).

Indication for and Time to ViV

The median time between procedures was shorter for ViTAVR compared with ViSAVR (3.2 versus 10 years; P<0.001; Table 2). The indication for ViV was almost identical for both groups (Figure S1). Average baseline prosthesis mean gradients were not different between primary AV replacement device categories (Figure 2). Prosthesis stenosis was present in 84.8% (n=84) of the study population. In these patients, the rate of severe prosthesis stenosis (mean prosthesis gradient >40 mm Hg) was 56% (n=47). Two patients presented with low-flow low-gradient prosthesis stenosis. In one ViTAVR patient, device dysfunction included both stenosis and PVL. For the remaining patients, indication for ViV could be categorized singularly as aortic stenosis, AR, or combined.

Procedural Characteristics and Device Success

ViV was performed via the transfemoral route in 87.9% of the patients (Table 2). There was no difference in ViV devices used (Figure S2). The rates of balloon- and self-expandable ViV devices were not different between groups (Figure 3). ViV size was larger in the ViTAVR group (P<0.001), with similar rates of postdilatation. When stratifying for the type of the ViV device used, higher rates of predilation in the ViTAVR group were found only for balloon-expandable ViV devices (P<0.001).

Procedural mortality was zero for all procedures. Valve positioning using a single device was accomplished in 100% and 97.3% for ViTAVR and ViSAVR, respectively (P=0.54). Paravalvular regurgitation > mild at day 1 was documented in 2 ViSAVR patients (compared with n=0 in ViTAVR). The overall incidence of residual mean gradients >19 mm Hg at day 1 was 30.5%. The rate of residual gradients was not different between groups. Consequently, device success was not different beween groups.

Early Safety and Clinical Efficacy

Hospital stay was significantly longer for ViTAVR patients (Table 3). Thirty-day survival for ViTAVR and ViSAVR was 96% and 94.6%, respectively (P=1.0). One ViSAVR patient died because of a procedure-related ventricular septum defect that could not be closed percutaneously. The remaining 3 ViSAVR patients died because of non–valve-related causes. One ViTAVR patient died following discharge to a community hospital because of unknown causes. For the survivors, the incidence of acute kidney injury, cerebrovascular event, and major bleeding within 30 days was not different between groups (overall incidences of 1%, 2%, and 3%, respectively).

There were no incidences of coronary obstruction requiring reintervention, major vascular complication, and valve-related dysfunction requiring repeated procedure. Consequently, early safety was 91.9% in the entire cohort (91.9% and 92% for ViSAVR and ViTAVR, respectively; P=1.0). There were higher rates of the combined end point of new major arrhythmia or new permanent pacemaker implantation within 30 days in the ViTAVR group (31.6% versus 6.8% for ViTAVR and ViSAVR, respectively; P=0.01). All but one pacemaker implantation in the ViTAVR patients was because of high-degree AV block; one patient received a pacemaker following ViTAVR because of preexisting sick-sinus syndrome; one patient showed new, hemodynamically significant atrial fibrillation. Considering only pacemaker implantation for higher-degree AV block group, rates of pacemaker implantation for ViTAVR were not statistically different compared with ViSAVR (16.7% versus 5.4%; P=0.1). When stratifying for the type of the ViV device used, higher rates of permanent pacemaker implantation in the ViTAVR group (42.9% versus 0%; P=0.026) were only observed for self-expandable ViV devices.

Mean transvalvular gradients at 30 days were lower for ViTAVR compared with ViSAVR (12.5 [IQR, 8.75–16.2] versus 16.4 [IQR, 13.0–20.2] mm Hg; P=0.043). Differences in peak transvalvular gradients did not reach statistical significance (24.0 [IQR, 17.2–29.8] versus 29.5 [IQR, 23.8–36.0] mm Hg; P=0.059) (Figure 4). Repeated measures analysis revealed the following: (1) no differences between groups, (2) a

Table 2. Procedural Characteristics

Characteristic	ViTAVR (N=25)	ViSAVR (N=74)	P Value (Overall)	N
Time since index procedure, y			<0.001	55
<5	18 (72.0)	5 (16.7)		
5–10	7 (28.0)	10 (33.3)		
>10	0 (0.00)	15 (50.0)		
Indication for ViV			0.754	99
AR	4 (16.0)	8 (10.8)		
AS	14 (56.0)	44 (59.5)		
Combined	7 (28.0)	22 (29.7)		
ViV access			0.455	98
Transapical	4 (16.7)	7 (9.46)		
Transfemoral	20 (83.3)	67 (90.5)		
ViV predilation			<0.001	99
No	15 (60.0)	73 (98.6)		
Yes	10 (40.0)	1 (1.35)		
ViV device			0.226	99
CoreValve	7 (28.0)	12 (16.2)		
CoreValve Evolut R	3 (12.0)	3 (4.05)		
Portico	0 (0.00)	2 (2.70)		
Sapien	3 (12.0)	17 (23.0)		
Sapien XT	3 (12.0)	19 (25.7)		
Sapien3	9 (36.0)	21 (28.4)		
ViV device self-expandable			0.164	99
Yes	10 (40.0)	17 (23.0)		
No	15 (60.0)	57 (77.0)		
ViV size, mm	26.0 (26.0–26.0)	23.0 (23.0–26.0)	<0.001	99
Postdilatation			0.547	98
No	16 (66.7)	56 (75.7)		
Yes	8 (33.3)	18 (24.3)		
Postprocedural gradient, mm Hg			0.349	95
<20	19 (79.2)	47 (66.2)		
>19	5 (20.8)	24 (33.8)		
Post-ViV PVL > mild			0.570	97
No	25 (100)	68 (94.4)		
Yes	0 (0.00)	4 (5.56)		
Device success			0.415	95
Accomplished	19 (79.2)	48 (67.6)		
Not accomplished	5 (20.8)	23 (32.4)		

Values are shown as median (interquartile range) for continuous variables and number (percentage) for categorical variables. Group differences are presented as overall P value. AR indicates aortic regurgitation; AS, aortic stenosis; PVL, paravalvular leakage; ViSAVR, valve in surgical aortic valve replacement; ViTAVR, valve in transcatheter aortic valve replacement; and ViV, valve-in-valve.

significant decrease of transvalvular gradients over time (P<0.001 for both mean and peak AV gradient), (3) a significant change in depression of transvalvular gradients within subjects over time (P<0.001 for both mean and peak AV gradient), and (4) no significant

interaction between the variables time and primary AV replacement device.

For ViTAVR, there were no differences with respect to hemodynamic outcome between balloon- and self-expandable ViV or primary AV replacement prostheses. Also, similar postprocedural gradients were observed in the ViSAVR group for small compared with large index devices (P=0.12; Figure S3). All-cause 1-year-mortality was 9.4% and 13.4% for the ViTAVR and ViSAVR groups, respectively (log-rank P=0.42; Figure 5). All but one death following discharge were non–cardiac related. One cardiac death was observed, which was not valve related.

DISCUSSION

This is the first study to compare ViV for degenerated surgical aortic bioprostheses in patients at high risk for repeated surgery against ViV for degenerated TAVR prostheses. According to Valve Academic Research Consortium-2 clinical end points, the main findings are the following: (1) ViTAVR is safe, with low incidence of periprocedural complications; (2) ViTAVR is effective in improving AV function, with low incidences of PVL; (3) ViTAVR provides slightly superior hemodynamic outcome, but similar rates of residual gradients >19 mm Hg; and (4) ViTAVR provides similar 1-year all-cause mortality compared with ViSAVR, despite increased surgical risk.

ViTAVR and ViSAVR Were Performed on Comparbale Study Populations

Data on ViSAVR demonstrate a decline of predicted surgical risk from 11.6% in 2011 to 7.4% in 2017.[4,5,7,19–22] This is in line with our study that reports on intermediate- to high-risk patients. By nature of the index procedure, the gap of predicted risk between ViTAVR and ViSAVR is likely going to persist, because both TAVR and bioprosthetic SAVR shift toward younger patients.[23]

Significant AR following TAVR is associated with impaired survival, but is relatively infrequent in current TAVR practice.[24] PVL has been shown to be more frequent for self- compared with balloon-expandable prostheses.[25] This disadvantage for self-expandable valves seems to diminish for newer-generation devices (presented by Dr Holger Thiele at the Transcatheter Cardiovascular Therapeutics meeting [TCT 2018], San Diego, CA, September 23, 2018). Consequently, PVL as an indication for ViTAVR may become relatively rare in the future, leading to ViTAVR and ViSAVR being performed in comparable patient populations.

The rate of PVL patients in our initial cohort of ViTAVR patients was close to numbers reported previously.[13] The exclusion of PVL patients showed that the
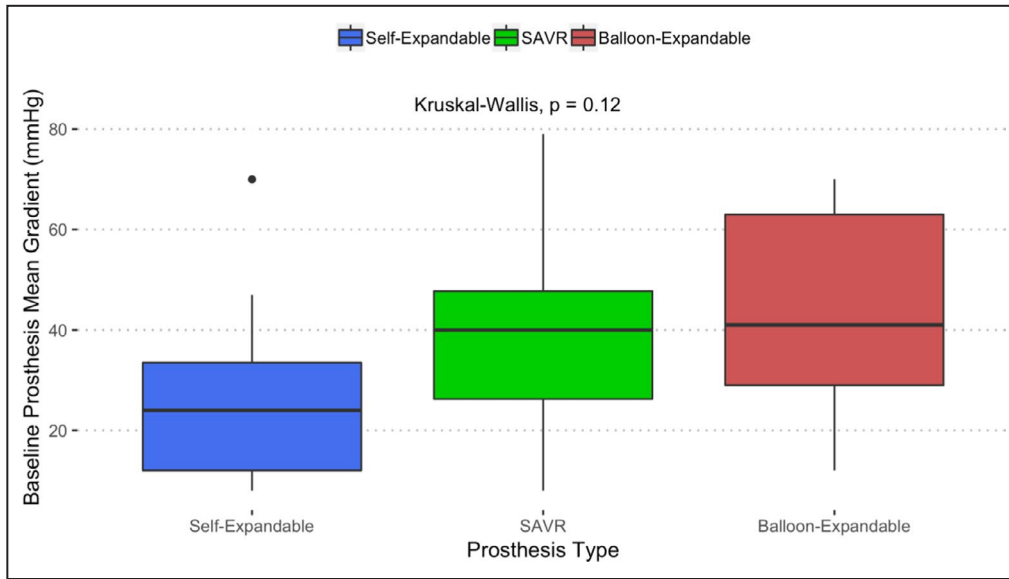
Figure 2. **Baseline mean gradient depending on type of index aortic valve replacement (AVR) device.**
Index AVR devices categorized into self-expandable (blue), balloon expandable (red), and surgical AVR (SAVR) (green). Kruskal-Wallis test for between-group differences.

indication for ViV becomes almost identical to ViSAVR, which, in turn, is in line with registry data.[5,7] Therefore, TAVR devices scheduled for ViV because of valve deterioration present similar hemodynamic compromises compared with their surgical counterparts. Pure prosthesis regurgitation as the indication for ViV is uncommon, and ≈75% of patients present with prosthesis stenosis.

ViTAVR Provides Slightly Superior Hemodynamics

Increased postprocedural gradients remain the Achilles heel of ViSAVR. It occurs in 26.8% to 37.0% of patients following ViV and is associated with increased mortality at 1 year.[7] No data exist for increased gradients following ViTAVR. Thus, our study
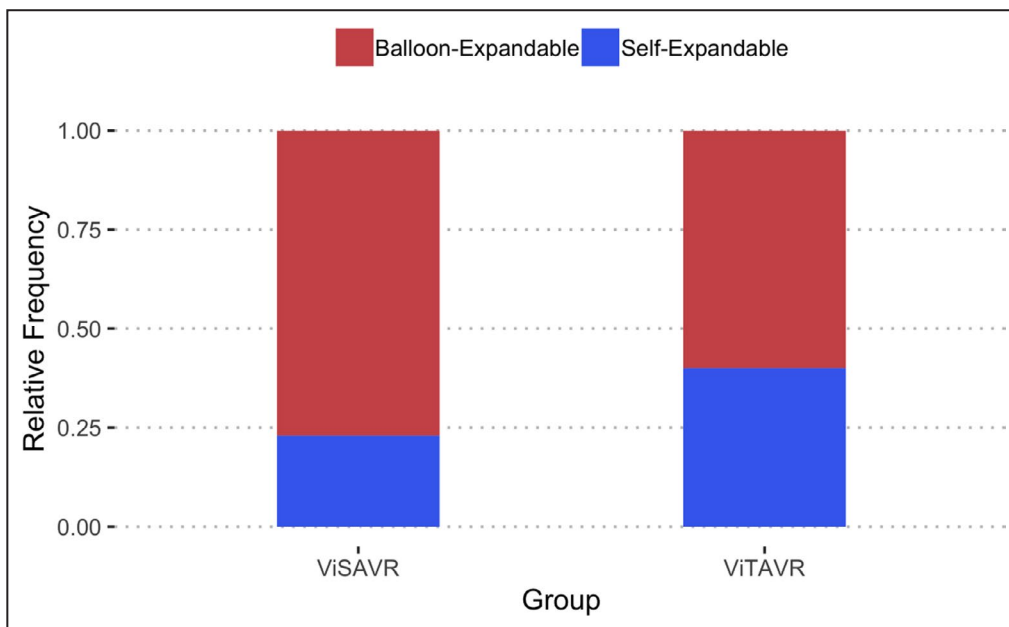

Figure 3. **Type of transcatheter aortic valve replacement device used.**
Comparison of valve-in-valve devices used in the valve in surgical aortic valve replacement (ViSAVR) (left) and the valve in transcatheter aortic valve replacement (ViTAVR) (right) groups.

Table 3. Clinical Outcome

Variable	ViTAVR (N=25)	ViSAVR (N=74)	P Value (Overall)	N
Day 1 ejection fraction, %	60.0 (50.0–65.0)	60.0 (47.0–65.0)	0.631	96
Day 1 PVL > mild			1.000	97
No	25 (100)	70 (97.2)		
Yes	0 (0.00)	2 (2.78)		
Day 1 ViV mean gradient, mm Hg	15.0 (11.8–17.5)	16.0 (11.0–21.0)	0.370	95
Day 1 ViV peak gradient, mm Hg	26.5 (19.8–36.2)	29.0 (20.5–38.0)	0.249	95
Postprocedural gradient category			0.572	95
Normal	19 (79.2)	52 (73.2)		
20–24 mm Hg	4 (16.7)	9 (12.7)		
25–29 mm Hg	1 (4.17)	4 (5.63)		
>29 mm Hg	0 (0.00)	6 (8.45)		
Hospital stay, d	9.00 (4.00–16.0)	3.00 (2.00–6.00)	<0.001	93
Death (hospital)			1.000	99
No	24 (96.0)	70 (94.6)		
Yes	1 (4.00)	4 (5.41)		
New permanent pacemaker implantation or major arrhythmia			0.011	78
No	13 (68.4)	55 (93.2)		
Yes	6 (31.6)	4 (6.78)		
Day 30 ejection fraction, %	59.0 (51.0–65.5)	61.0 (54.0–66.0)	0.810	67
Day 30 PVL > mild			1.000	69
No	16 (100)	51 (96.2)		
Yes	0 (0.00)	2 (3.77)		
Day 30 ViV mean gradient, mm Hg	12.5 (8.75–16.2)	16.4 (13.0–20.2)	0.043	68
Day 30 ViV peak gradient, mm Hg	24.0 (17.2–29.8)	29.5 (23.8–36.0)	0.059	66
Postprocedural gradient at 30 d, mm Hg			0.201	68
<20	14 (87.5)	35 (67.3)		
>19	2 (12.5)	17 (32.7)		

Values are shown as median (interquartile range) for continuous variables and number (percentage) for categorical variables. Group differences are presented as overall P value. PVL indicates paravalvular leakage; ViSAVR, valve in surgical aortic valve replacement; ViTAVR, valve in transcatheter aortic valve replacement; and ViV, valve-in-valve.

is the first to demonstrate similar rates of increased postprocedural gradients following ViTAVR. This result is surprising because both the design of TAVR devices and the size of TAVR devices that presented for ViTAVR favored no incidence of residual gradients. However, 3 considerations have to be noted. First, the definition of increased gradients is based on data obtained by ViV for failed surgical aortic bioprosthesis. It is unclear whether a similar cutoff should be applied also for ViTAVR with respect to an association with mortality. Second, the variable of increased gradients categorizes a continuous variable into a binary one, with no further differentiation for even higher gradients. Third, leaflet abnormalities, including thickening and subclinical thrombosis, have been shown to be more frequent in transcatheter compared with surgical aortic bioprostheses.[26,27] This could possibly contribute to decreased prosthesis opening area following ViTAVR despite greater

index valve sizes and the lack of a surgical sewing ring.

Thus, our study shows a tendency toward improved hemodynamics at 30 days for the ViTAVR compared with the ViSAVR group. As device success depends on the absence of increased residual gradients, however, further in vitro studies are required to deepen our understanding of the causes and contributors of increased gradients following both ViSAVR and ViTAVR.

Increased Rates of Pacemaker Implantation With Similar 1-Year Survival

ViTAVR is a safe procedure with zero procedural mortality and no incidence of valve malpositioning. Furthermore, it is safe with respect to hospital death, major vascular or cerebrovascular events, acute kidney injury, and major bleeding. However, a combined
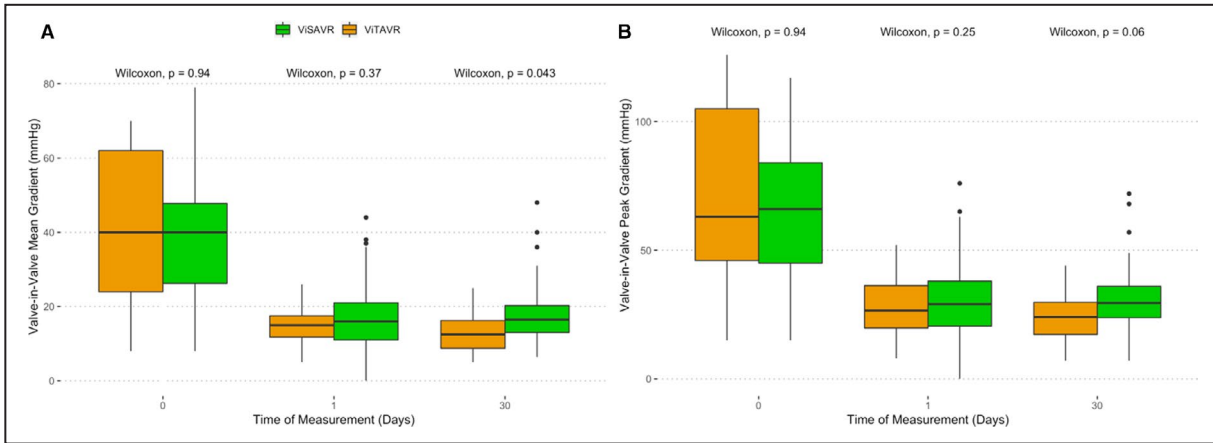
Figure 4.   Hemodynamic outcome.
A, Valve-in-valve mean gradients. **B**, Valve-in-valve peak gradients. Green=valve in surgical aortic valve replacement (ViSAVR), and orange=valve in transcatheter aortic valve replacement (ViTAVR). See Results section with regard to repeated-measures analysis.

end point of new arrhythmia or new pacemaker implantation occurred frequently. New pacemaker implantation following native TAVR remains a common procedure even for new-generation devices.

Compared with native TAVR, ViSAVR shows lower rates of permanent pacemaker implantation, in part likely because of a protective ability of the sewing ring toward conductive structures. The incidence of
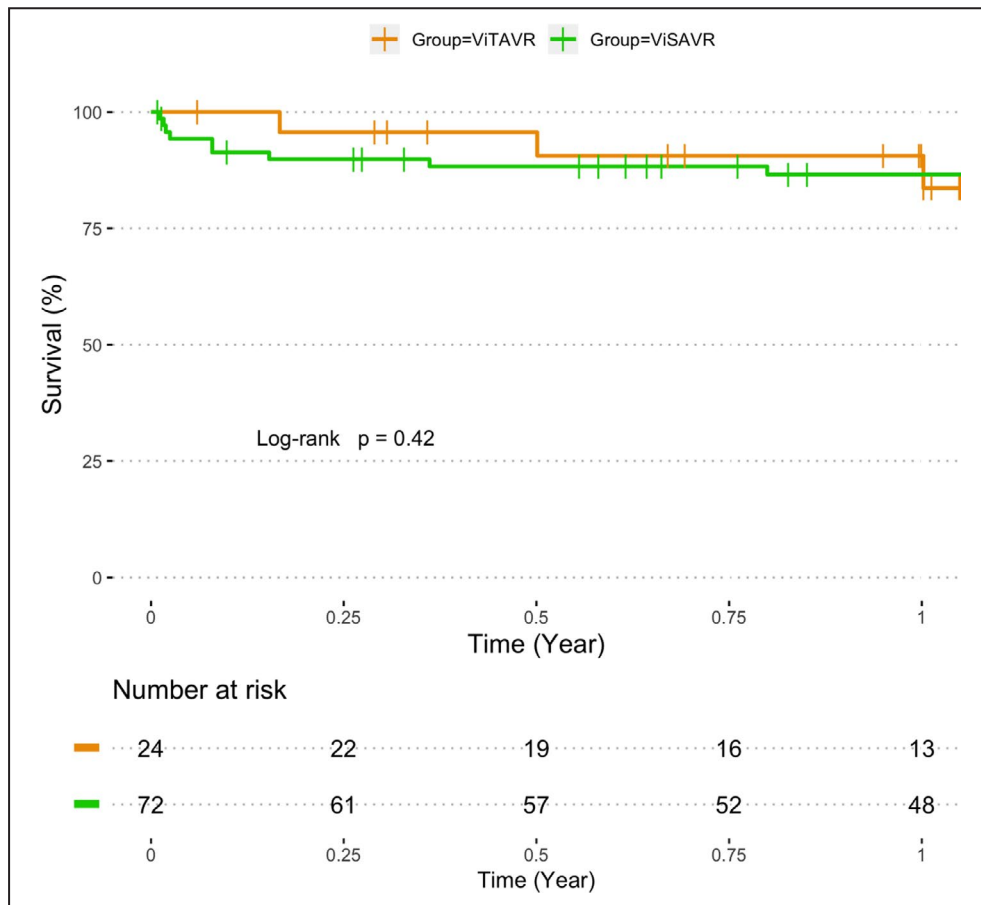
Figure 5.   One-year-survival.
Survival curve of cumulative 1-year all-cause mortality for valve in surgical aortic valve replacement (ViSAVR) (green) and valve in transcatheter aortic valve replacement (ViTAVR) (orange).

new permanent pacemaker of 5.4% for ViSAVR in our study is in line with numbers previously reported; the incidence of new pacemaker implantation following valve-deteriorated ViTAVR of 16.7% is higher than reported by Barbanti et al[13] and slightly higher compared with current data on native trileaflet TAVR. Given that ViTAVR places a device into 2 calcified structures (ie, native calcified AV and deteriorated TAVR device), greater amounts of calcified elements compared with ViSAVR pushed radially may be a contributor.

Despite a higher predicted surgical risk, 1-year survival and clinical outcome were not different for ViTAVR, although longer duration of follow-up is required in future studies.

Limitations

The main limitation of this study is the retrospective, observational character. Data collection was based on clinical documentation and review of selected variables, leading to inconsistencies with respect to data collection and quality. Second, only 2 surgical aortic bioprostheses were used for comparison collected at a single center. Thus, institutional bias cannot be excluded. Finally, although our study provides the largest series of deteriorated TAVR devices scheduled for ViV compared with ViSAVR, the sample size is still small and our study may therefore be underpowered to detect differences to a statistically significant degree.

CONCLUSIONS

For intermediate- to high-risk patients, ViTAVR provides acceptable clinical outcome compared with ViSAVR. Hemodynamic outcome seems slightly better, but device success rates and 1-year all-cause mortality may not be different.

ARTICLE INFORMATION

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Supplementary Materials

Figures S1–S3

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SUPPLEMENTAL MATERIAL

Figure S1. Indication for Valve-in-Valve after Exclusion of PVL-Patients.

A

Mode of Dysfunction ■ AR ■ AS ■ combined

1

B

Mode of Dysfunction ■ AR ■ AS ■ combined

1
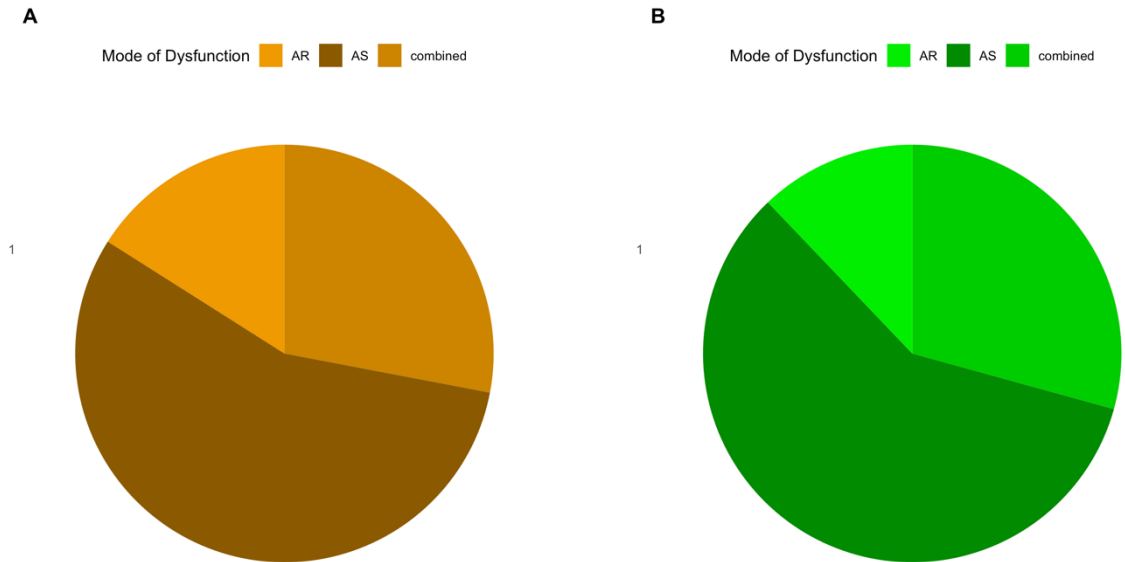
Distribution of Indication for ViTAVR (n=25). B, Distribution of Indication for ViSAVR (n=74). ViTAVR=Valve-In-valve for failed Transcatheter Aortic Valve Replacement, ViSAVR: Valve-In-valve for failed Surgical Aortic Valve Replacement, AR= Aortic Regurgitation; AS=Aortic Stenosis.

Figure S2. Valve-in-Valve Devices Used. Legend: Relative frequencies of Valve-in-Valve Devices for ViSAVR (left) and ViTAVR (right).
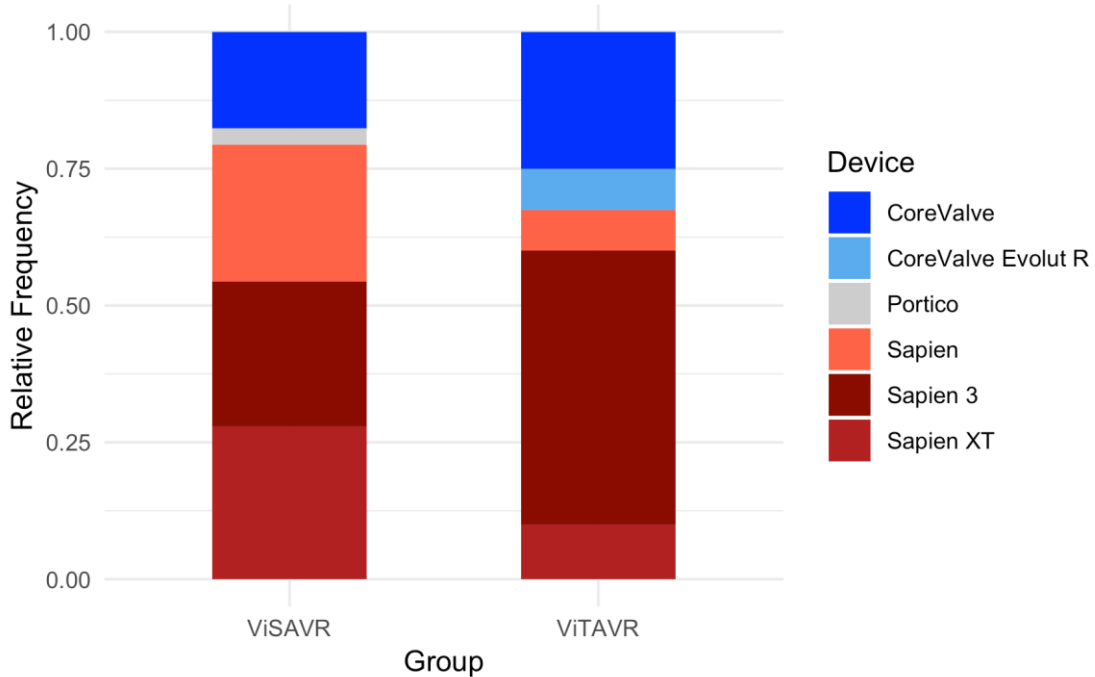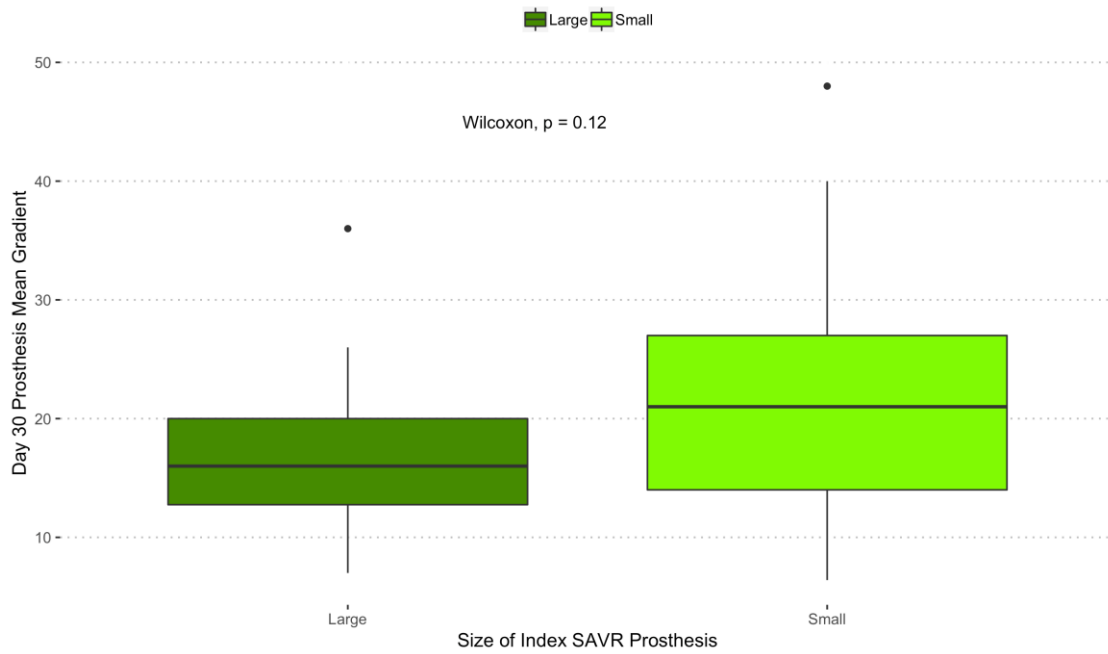
Figure S3. Hemodynamic Outcome Depending on Size of Index Prosthesis. Legend: Hemodynamic Outcome at 30 Days following valve-in-valve for large (left, >19mm true internal diameter) versus small (right) index SAVR devices in the ViSAVR group.

SAVR: Surgical Aortic Valve Replacement, Dark Green: Large SAVR Prosthesis, Light Green=Small SAVR Prosthesis.