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TAVR for Failed Surgical Aortic Bioprostheses Using a Self-Expanding Device

1-Year Results From the Prospective VIVA Postmarket Study

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ABSTRACT

OBJECTIVES The VIVA (Valve in Valve) trial was designed to systematically and prospectively collect data regarding the use of transcatheter aortic valve replacement in patients with failing surgical aortic bioprostheses at high-risk for reoperation.

BACKGROUND Surgical aortic valve replacement has been the standard of care in symptomatic patients with aortic valve disease. However, bioprosthetic valves degenerate over time, requiring redo surgery.

METHODS VIVA is an international, observational, single-arm, postmarket study conducted at 23 sites that enrolled 202 patients with symptomatic degeneration of an aortic bioprosthesis eligible for elective treatment with a CoreValve or Evolut R self-expanding transcatheter aortic valve.

RESULTS Patients were elderly (mean age 79.9 years), 47.5% were men, and they had a mean Society of Thoracic Surgeons score of 6.6%. Although 41.8% of patients had surgical bioprostheses with labeled size ≤21 mm, valve hemodynamic parameters were markedly improved from baseline (mean aortic valve gradient 35.0 ± 16.3 mm Hg) to discharge (17.5 ± 8.6 mm Hg) and were sustained at 1 year (15.5 ± 7.5 mm Hg). At 1 year, total aortic regurgitation greater than mild was measured in 1.1% of patients. Clinical outcomes at 30 days demonstrated low mortality (2.5%), no disabling strokes, a 0.5% rate of acute kidney injury, and an 8.0% rate of new pacemaker implantation. At 1 year, the mortality rate remained low (8.8%), with 1 disabling stroke (0.6%). Five patients (2.5%) experienced coronary artery obstructions, 3 during and 1 immediately after the procedure and 1 several months later.

CONCLUSIONS Degenerated surgical bioprostheses can be safely treated with the CoreValve or Evolut R platform using the catheter-based valve-in-valve procedure. Excellent 1-year clinical and hemodynamic outcomes were achieved in this real-world patient population. (CoreValve VIVA Study Evaluation of the Clinical Outcomes of CoreValve in Degenerative Surgical Aortic Bioprosthesis; NCT02209298) (J Am Coll Cardiol Intv 2019;12:923-32)

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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

VIV = valve-in-valve

Surgical aortic valve replacement has been the treatment of choice for elderly patients presenting with aortic stenosis or regurgitation, but it results over time in degeneration of the bioprosthesis. Reoperation is often the preferred approach for bioprosthesis degeneration but carries substantial surgical risk (1–4). A growing body of evidence now demonstrates that transcatheter aortic valve replacement (TAVR) is a less-invasive alternative to redo surgical aortic valve replacement for patients who are at high surgical risk (5–10). When patients with failed surgical bioprostheses cannot undergo reoperation because of age or comorbidities, TAVR inside a failed surgical bioprosthesis, or valve-in-valve (VIV), represents a less invasive therapeutic strategy (11–13). Most data on VIV interventions were derived from retrospective self-reported registries (11). The aim of the present VIVA (Valve in Valve) trial was to prospectively evaluate real-world clinical and hemodynamic outcomes among patients with failing surgical aortic bioprostheses who underwent TAVR with a self-expanding transcatheter heart valve (THV): the CoreValve or Evolut R (Medtronic, Minneapolis, Minnesota).

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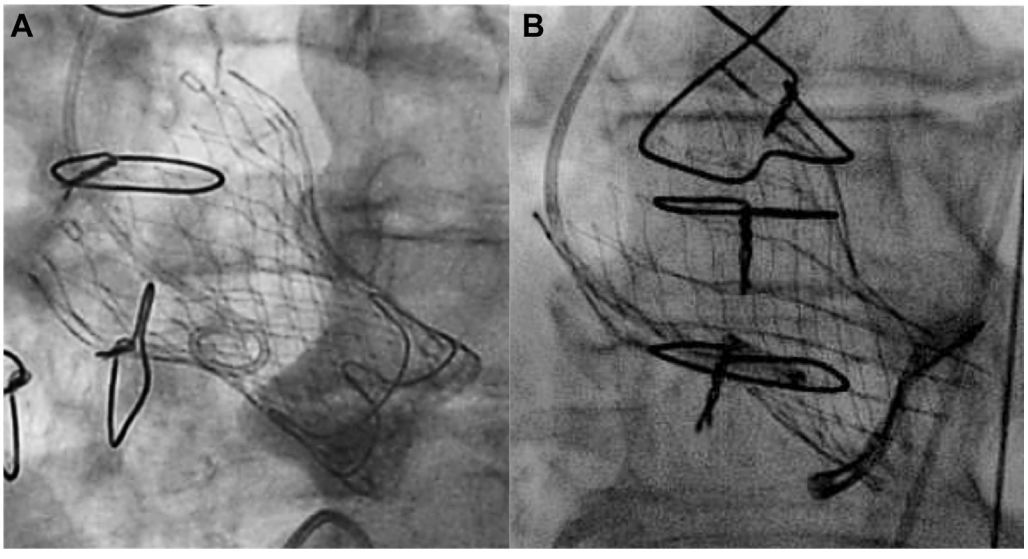
METHODS

STUDY DESIGN. VIVA is an observational, single-arm, postmarket multicenter study conducted at 23 sites in France, Germany, Israel, and Italy (Online Table 1). All patients were informed of the nature of the procedure and study, provided written informed consent to participate, and were willing and able to comply with study requirements, including 24 months of follow-up. The study complied with the Declaration of Helsinki, and the research protocol was approved by each site's ethics committee according to individual

FIGURE 1 Fluoroscopic Aspects of the Valve-in-Valve Intervention



(A) CoreValve transcatheter heart valve (THV) in a Perimount bioprosthesis. **(B)** Evolut R THV in a Mitroflow bioprosthesis.

adviser for Edwards Lifesciences. Dr. Teiger has received personal fees from Medtronic during conduct of the study. Dr. Li is an employee of and shareholder in Medtronic. Dr. Harnath has received payments for clinical study involvement from Medtronic; has received traveling compensation from Medtronic; and is a proctor and consultant for Medtronic. Dr. Manigold is a consultant and proctor for Medtronic. Dr. Oh has a consulting contract with Medtronic; and has received grants paid to his institution. Dr. Schäfer has received proctor speaking honoraria, travel support, and grant support from Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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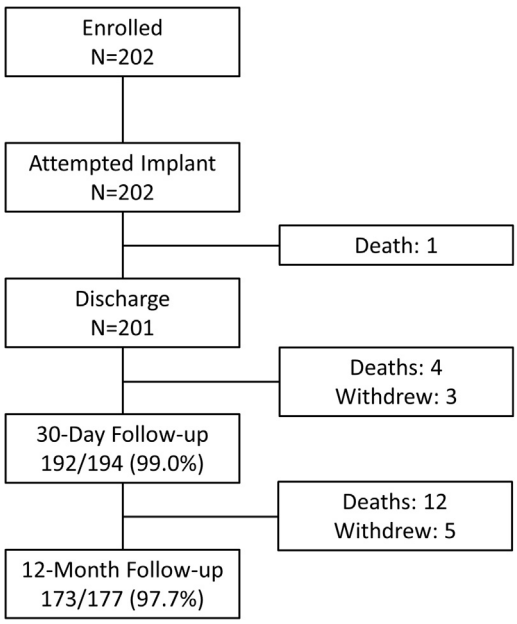
FIGURE 2 Patient Flow Diagram



national requirements. Independent site management, monitoring and clinical events committee adjudication were performed by the Cardiovascular European Research Center (Massy, France). For a list of VIVA investigators, please see the Online Appendix.

INCLUSION AND EXCLUSION. Adults (>18 years of age) with symptomatic degeneration of an aortic bioprosthesis (stenosis and/or regurgitation) who were acceptable candidates for elective treatment with a self-expanding transcatheter aortic valve were eligible for inclusion. Patients were required to have logistic European System for Cardiac Operative Risk Evaluation scores >20% or Society of Thoracic Surgeons scores >10% or presence of comorbidities contraindicating redo surgery as assessed by at least 1 cardiac surgeon or patients in whom the heart team assessed redo surgery at high risk. Patients were excluded because of any of the following: antiplatelet and/or anticoagulant therapy was contraindicated; the heart team considered the risk of TAVR too high, particularly with augmented risk for coronary occlusion; prior or active endocarditis on failed bioprosthesis; other medical illness associated with limited life expectancy (i.e., <1 year); left ventricular ejection fraction <20%, cardiogenic shock, or hemodynamic compromise requiring vasopressors or inotrope medications or mechanical support devices; severe mitral disease associated with severe pulmonary hypertension; acute coronary syndrome <7 days

TABLE 1 Baseline Demographics

	All (N = 202)	Stenosis (n = 114)	Regurgitation (n = 46)	Combined (n = 42)	p Value
Age (yrs)	79.9 ± 7.2	79.4 ± 7.1	80.1 ± 8.6	81.1 ± 5.6	0.45
BSA (m^2)	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	1.8 ± 0.2	0.78
Male	96 (47.5)	51 (44.7)	27 (58.7)	18 (42.9)	0.22
STS-PROM (%)	6.6 ± 5.1	6.4 ± 4.6	6.1 ± 4.9	7.6 ± 6.5	0.34
Logistic EuroSCORE (%)	25.0 ± 14.3	23.7 ± 12.6	27.7 ± 17.3	25.8 ± 14.9	0.26
Diabetes	53 (26.2)	36 (31.6)	7 (15.2)	10 (23.8)	0.10
Hypertension	167/200 (83.5)	94/114 (82.5)	39/44 (88.6)	34/42 (81.0)	0.57
Peripheral vascular disease	28 (13.9)	15 (13.2)	6 (13.0)	7 (16.7)	0.84
Previous stroke	10 (5.0)	10 (8.8)	0 (0.0)	0 (0.0)	0.02
Previous transient ischemic attack	5/201 (2.5)	2 (1.8)	2 (4.3)	1/41 (2.4)	0.60
Chronic lung disease/COPD	42 (20.8)	26 (22.8)	5 (10.9)	11 (26.2)	0.15
Percutaneous coronary intervention	54 (26.7)	36 (31.6)	11 (23.9)	7 (16.7)	0.16
Balloon valvuloplasty	12 (5.9)	9 (7.9)	0 (0.0)	3 (7.1)	0.12
Previous myocardial infarction	22 (10.9)	15 (13.2)	3 (6.5)	4 (9.5)	0.53
NYHA functional class					0.54
I	7/198 (3.5)	7/113 (6.2)	0/45 (0.0)	0/40 (0.0)	
II	51/198 (25.8)	26/113 (23.0)	11/45 (24.4)	14/40 (35.0)	
III	108/198 (54.5)	64/113 (56.6)	25/45 (55.6)	19/40 (47.5)	
IV	32/198 (16.2)	16/113 (14.2)	9/45 (20.0)	7/40 (17.5)	

Values are mean ± SD, n (%), or n/N (%). Denominators are presented if different from column headers.

BSA = body surface area; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

TABLE 2 Surgical Valve Characteristics

	All (N = 202)	Stenosis (n = 114)	Regurgitation (n = 46)	Combined (n = 42)	p Value
Surgical valve age (yrs)	9.3 ± 4.4	8.9 ± 4.4	9.7 ± 3.5	9.9 ± 5.0	0.34
Failed bioprosthetic surgical valve					0.04
Stented	188 (93.1)	108 (94.7)	39 (84.8)	41 (97.6)	
Stentless	14 (6.9)	6 (5.3)	7 (15.2)	1 (2.4)	
Homograft	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Bioprosthesis labeled size (mm)	22.7 ± 2.1	22.6 ± 2.1	23.2 ± 2.2	22.5 ± 2.0	0.17
≤21	84/201 (41.8)	48/113 (42.5)	16 (34.8)	20 (47.6)	0.15
>21 and <25	65/201 (32.3)	39/113 (34.5)	12 (26.1)	14 (33.3)	
≥25	52/201 (25.9)	26/113 (23.0)	18 (39.1)	8 (19.0)	
Calcified aorta					0.07
None	71/159 (44.7)	34/85 (40.0)	22/41 (53.7)	15/33 (45.5)	
Mild	56/159 (35.2)	28/85 (32.9)	17/41 41.5	11/33 (33.3)	
Moderate	25/159 (15.7)	16/85 (18.8)	2/41 (4.9)	7/33 (21.2)	
Severe	7/159 (4.4)	7/85 (8.2)	0/41 (0.0)	0/33 (0.0)	
Porcelain aorta	0/159 (0.0)	0/85 (0.0)	0/41 (0.0)	0/33 (0.0)	
Bioprosthesis internal diameter (mm)	20.9 ± 2.7	21.0 ± 2.7	21.0 ± 3.0	20.4 ± 2.3	0.44
<20	70/171 (40.9)	40/96 (41.7)	15/40 (37.5)	15/35 (42.9)	0.72
≥20 and <23	60/171 (35.1)	32/96 (33.3)	14/40 (35.0)	14/35 (40.0)	
≥23	41/171 (24.0)	24/96 (25.0)	11/40 (27.5)	6/35 (17.1)	

Values are mean ± SD, n (%), or n/N (%). Denominators are presented if different from column headers.

TABLE 3 Procedural Characteristics

	All (N = 202)	Stenosis (n = 114)	Regurgitation (n = 46)	Combined (n = 42)	p Value
Total procedure time (min)	64.5 (48.0–90.0)	60.0 (45.0–84.0)	72.0 (56.0–102.0)	62.0 (49.0–85.0)	0.12
Anesthesia type					0.04
Local	84 (41.6)	50 (43.9)	13 (28.3)	21 (50.0)	
General	47 (23.3)	20 (17.5)	13 (28.3)	14 (33.3)	
Sedation	71 (35.1)	44 (38.6)	20 (43.5)	7 (16.7)	
Access site					0.03
Iliofemoral	195 (96.5)	113 (99.1)	44 (95.7)	38 (90.5)	
Subclavian/axillary	4 (2.0)	0 (0.0)	1 (2.2)	3 (7.1)	
Transcarotid	2 (1.0)	1 (0.9)	1 (2.2)	0 (0.0)	
Direct aortic	1 (0.5)	0 (0.0)	0 (0.0)	1 (2.4)	
Percutaneous closure device used	186/201 (92.5)	112 (98.2)	39 (84.8)	35/41 (85.4)	<0.001
Pre-TAVR balloon valvuloplasty	28 (13.9)	27 (23.7)	0 (0.0)	1 (2.4)	<0.001
Post-TAVR balloon valvuloplasty	42 (20.8)	31 (27.2)	7 (15.2)	4 (9.5)	0.03
Other concomitant procedures performed	15 (7.4)	8 (7.0)	3 (6.5)	4 (9.5)	0.87
THV retrieved	4 (2.0)	1 (0.9)	2 (4.3)	1 (2.4)	0.22
≥2 valves implanted	2 (1.0)	0 (0.0)	2 (4.3)	0 (0.0)	0.09
CoreValve					0.48
23 mm	6/19 (31.6)	2/6 (33.3)	2/7 (28.6)	2/6 (33.3)	
26 mm	10/19 (52.6)	4/6 (66.7)	5/7 (71.4)	1/6 (16.7)	
29 mm	3/19 (15.8)	0/6 (0.0)	0/7 (0.0)	3/6 (50.0)	
31 mm	0/19 (0.0)	0/6 (0.0)	0/7 (0.0)	0/6 (0.0)	
Evolut R*					0.25
23 mm	122/182 (67.0)	77/108 (71.3)	21/38 (55.3)	24/36 (66.7)	
26 mm	44/182 (24.2)	21/108 (19.4)	13/38 (34.2)	10/36 (27.8)	
29 mm	16/182 (8.8)	10/108 (9.3)	4/38 (10.5)	2/36 (5.6)	

Values are median (interquartile range), n (%), or n/N (%). Denominators are presented if different from column headers. *1 patient was not implanted with a THV.

TAVR = transcatheter aortic valve replacement; THV = transcatheter heart valve.

before intervention; current participation in another investigational drug or device study; significant paravalvular regurgitation; and patients in whom internal diameter prosthesis was ≤17 mm.

ENDPOINTS. The primary safety endpoint was cardiovascular death at 30 days post-procedure, expected a priori to be <10%. The primary efficacy endpoint was lack of significant aortic stenosis (mean gradient >40 mm Hg) or insufficiency (greater than moderate severity) at 1 year post-procedure using clinical evaluation and echocardiography. Secondary endpoints were adjudicated per Valve Academic Research Consortium 2 (14) and included access-site complications, major bleeding, stroke, acute kidney injury stage III, new pacemaker implantation, and post-implantation aortic gradient. Patients were assessed at baseline, procedure, discharge, 30 days, 6 months, and 12 months.

ECHOCARDIOGRAPHIC ANALYSIS. Serial echocardiograms were recorded at screening, discharge, and 12 months post-procedure. Independent echocardiographic analysis was provided by a central core laboratory (Mayo Clinic, Rochester, Minnesota) (15).

DEVICE AND PROCEDURE. The self-expanding CoreValve (n = 19) or Evolut R (n = 183) THV was used in all 202 patients (Figure 1). Features of these THVs have been extensively described elsewhere (16). Transfemoral, subclavian, transcarotid, and direct aortic access were allowed. Prosthesis size, access route, and anesthesia type were left to operating team discretion.

STATISTICAL ANALYSIS. All patients undergoing attempted VIV implantation constituted the primary analysis group for this report. Categorical variables were compared using chi-square tests unless there were observed cell counts of <5, in which case the Fisher exact test was used. Continuous variables are presented as mean ± SD or as median (interquartile range) and were compared using 2-sample Student's *t*-tests or analysis-of-variance *F* test (for 3 or more group comparisons). Kaplan-Meier estimates were used to perform clinical outcome time-to-event analysis. The log-rank test was used to assess possible differences between or among subgroups in time-to-event data. All testing used a 2-sided alpha level of 0.05. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

PATIENT CHARACTERISTICS. A total of 202 patients underwent attempted implantation (Figure 2), and patients were followed for a median of 13.2 months (interquartile range: 12.0 to 24.0 months). Patient demographics are reported in Table 1. Nearly one-half of patients were men (47.5%), with mean age of 79.9 ± 7.2 years, a mean logistic European System for Cardiac Operative Risk Evaluation score of 25.0 ± 14.3%, and a mean Society of Thoracic Surgeons score of 6.6 ± 5.1%. The most prominent comorbidities were hypertension (83.5%) and chronic lung disease or chronic obstructive pulmonary disease (20.8%). Patients were commonly (70.7%) in New York Heart Association functional class III or IV.

SURGICAL VALVE CHARACTERISTICS. Surgical valve characteristics are detailed in Table 2. Most failed surgical prostheses were stented valves (93.1%), with a mean time until treatment of 9.3 ±

4.4 years. Slightly more than one-half of the surgical bioprostheses failed because of stenosis pathology (56.4%). Most surgical valves were small, with 41.8% having manufacturer external label sizes of 21 mm or less. The most common types of failed bioprostheses in this series were Mitroflow (37.1%) and Perimount or Magna (28.7%) (Online Figure 1).

PROCEDURAL OUTCOMES. In total, 201 of 202 patients (99.5%) were successfully implanted with self-expanding CoreValve or Evolut R prostheses. In 1 patient, implantation was initially attempted using VIV, but because the implant was not successful because of reported coronary occlusion with no relevant stenosis, the procedure was stopped, and the patient was treated using a Perceval surgical valve. The CoreValve THV was implanted in 19 of 202 patients (9.4%), while the Evolut R THV was implanted in 182 of 202 patients (90.1%) (**Figure 1**). The 23-mm THV was used most frequently (63.7%), and the iliofemoral route was chosen for access in 96.5% of cases. General anesthesia was used infrequently (23.3%) compared with local anesthesia or conscious sedation. Pre-implantation balloon valvuloplasty was used in only 13.9% of cases, while post-implantation valvuloplasty was needed in 20.8% of cases (**Table 3**).

The THV was retrieved in 4 patients (2.0%) after several unsuccessful attempts; 3 patients were successfully implanted with new THVs, and the fourth had his THV removed and reloaded for final successful deployment. Two patients (1.0%) required implantation of a second THV within the first for malpositioning. One of these patients reportedly had evidence of valve embolization, as the first THV immediately migrated above the annulus during deployment. It was captured with a snare and maintained in the ascending aorta, with a second THV successfully implanted across it. In the second patient, the first THV was deployed too high and corrected with deeper implantation of a second THV. Overall, the repositioning feature of the Evolut R THV was used in 32 of 183 patients (17.5%).

CLINICAL OUTCOMES AT 30 DAYS. At 30 days, the rate of all-cause mortality, as well as cardiovascular mortality, was 2.5%. All 5 deaths occurred in patients with stenosis as the predominant failure mode of their surgical bioprostheses. Two deaths followed myocardial infarctions, 1 of which was caused by procedural occlusion of the left main coronary artery, 1 due to cardiogenic shock and 1 to cardiac arrest. A fifth patient experienced death due to multiorgan failure. The 30-day stroke rate was 3.0%, and no strokes were considered disabling. The vascular complication rate was 7% (minor access-site complications, 5.5%; major access-site complications, 1.5%) according to Valve Academic Research Consortium 2 criteria. The rate of new permanent pacemaker implantation was 8.0%. There were 3 coronary obstructions during the procedure (1 of which resulted in death, mentioned earlier) and 1 additional obstruction occurring immediately after the procedure (2.0%) (**Table 4**). All four of these coronary obstructions occurred in patients presenting with Mitroflow surgical valves and implanted with 23-mm Evolut R THVs. At 30 days, there were no reported cases of prosthetic valve endocarditis, and 1 case (0.5%) of prosthetic valve thrombosis evidenced by increased gradients and mobile material observed on

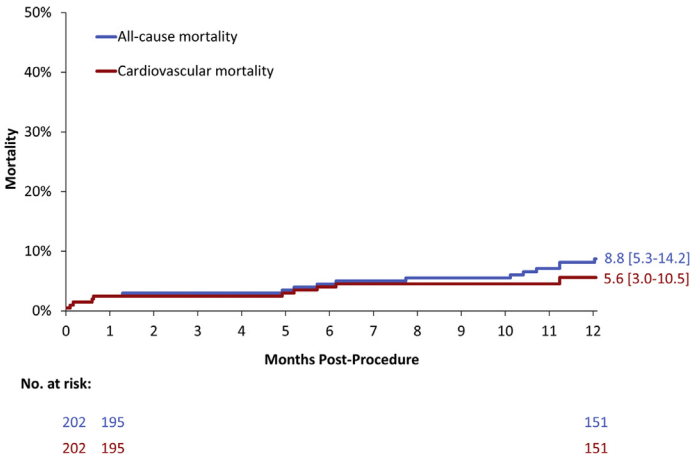
TABLE 4 Clinical Outcomes

	All (N = 202)	Stenosis (n = 114)	Regurgitation (n = 46)	Combined (n = 42)	p Value
30-day clinical outcomes					
All-cause mortality	5 (2.5)	5 (4.4)	0 (0.0)	0 (0.0)	0.14
Cardiovascular	5 (2.5)	5 (4.4)	0 (0.0)	0 (0.0)	0.14
Myocardial infarction	1 (0.5)	0 (0.0)	0 (0.0)	1 (2.4)	0.15
Access-site complication	14 (7.0)	9 (7.9)	2 (4.3)	3 (7.1)	0.72
Major access-site complication	3 (1.5)	2 (1.8)	0 (0.0)	1 (2.4)	0.61
VARC bleeding	30 (14.9)	16 (14.1)	9 (19.6)	5 (11.9)	0.58
Life-threatening bleeding	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Major bleeding	14 (7.0)	8 (7.1)	4 (8.7)	2 (4.8)	0.77
Acute kidney injury stage I	1 (0.5)	1 (0.9)	0 (0.0)	0 (0.0)	0.68
Stage II or III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Prosthetic valve endocarditis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Prosthetic valve thrombosis	1 (0.5)	1 (0.9)	0 (0.0)	0 (0.0)	0.68
Coronary artery obstruction requiring intervention	4 (2.0)	2 (1.8)	2 (4.3)	0 (0.0)	0.33
All stroke	6 (3.0)	5 (4.4)	1 (2.2)	0 (0.0)	0.34
Disabling stroke	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
New pacemaker implantation*	16 (8.0)	10 (8.9)	2 (4.3)	4 (9.5)	0.57
12-month clinical outcomes					
All-cause mortality	17 (8.8)	11 (10.1)	3 (6.5)	3 (7.3)	0.72
Cardiovascular	11 (5.6)	9 (8.2)	0 (0.0)	2 (5.0)	0.13
Myocardial infarction	1 (0.5)	0 (0.0)	0 (0.0)	1 (2.4)	0.15
Access-site complication	14 (7.0)	9 (7.9)	2 (4.3)	3 (7.1)	0.72
Major access-site complication	3 (1.5)	2 (1.8)	0 (0.0)	1 (2.4)	0.61
VARC bleeding	35 (17.6)	18 (16.1)	11 (23.9)	6 (14.4)	0.44
Life-threatening bleeding	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Major bleeding	18 (9.1)	9 (8.1)	6 (13.0)	3 (7.2)	0.57
Acute kidney injury stage I	1 (0.5)	1 (0.9)	0 (0.0)	0 (0.0)	0.68
Stage II or III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Prosthetic valve endocarditis	1 (0.5)	1 (1.0)	0 (0.0)	0 (0.0)	0.65
Prosthetic valve thrombosis	2 (1.0)	1 (0.9)	1 (2.2)	0 (0.0)	0.61
Coronary artery obstruction requiring intervention	5 (2.5)	2 (1.8)	2 (4.3)	1 (2.4)	0.64
All stroke	12 (6.2)	9 (8.3)	2 (4.4)	1 (2.6)	0.35
Disabling stroke	1 (0.6)	1 (1.1)	0 (0.0)	0 (0.0)	0.66
New pacemaker implantation*	20 (10.1)	14 (12.8)	2 (4.3)	4 (9.5)	0.30

Values are number of patients with events (%), depicted as Kaplan-Meier event rates. *Includes patients with baseline pacemaker.

NA = not applicable; VARC = Valve Academic Research Consortium.

FIGURE 3 All-Cause Mortality and Cardiovascular Mortality



Rates are reported as Kaplan-Meier percentages (95% confidence intervals).

echocardiography; the patient was treated with heparin and warfarin, with improvement of gradients and imaging findings.

CLINICAL OUTCOMES AT 12 MONTHS. There were 12 additional deaths between 30 days and 12 months, resulting in a 12-month all-cause mortality rate of 8.8%; cardiovascular mortality was only 5.6% at 1 year (**Figure 3**). Mortality did not significantly differ when stratified by surgical bioprosthesis size (**Central Illustration**). The overall 12-month stroke rate was 6.2%, with 1 stroke deemed disabling (0.6%), and no instances of leaflet thickening or immobility were noted. After 30 days, 2 of the 6 strokes were hemorrhagic in origin and 4 were embolic, of which 1 was in the patient converted to a Perceval implantation. The 12-month rate of new pacemaker implantation was 10.1%. No significant differences were noted between any clinical outcomes by failure mode of the surgical bioprosthesis. One patient had a late coronary artery occlusion that was identified 5 months after VIV intervention, treated with coronary artery bypass graft. Coronary angiography showed left main coronary thrombosis within a treated Freestyle bioprosthesis (**Table 4**). There was 1 reported case of prosthetic valve endocarditis (0.5%) at 12 months in which the patient recovered with antibiotics and 1 additional case of prosthetic valve thrombosis (1.0%) in a patient with a Freestyle bioprosthesis manifested by a significant increase in gradients and dyspnea. Following initiation of warfarin, the gradients decreased to normal values and symptoms improved.

ECHOCARDIOGRAPHIC FINDINGS. The mean gradient across the aortic valve was reduced from 35.0 ± 16.3 mm Hg to 17.5 ± 8.6 mm Hg and 15.5 ± 7.5 mm Hg at baseline, discharge, and 1 year, respectively. Effective orifice area increased from 1.1 ± 0.5 cm^2 to 1.3 ± 0.5 cm^2 to 1.4 ± 0.6 cm^2 (**Figure 4A**, Online Table 2). Although no differences in post-procedural mean gradient were noted according to surgical bioprosthesis failure mode (**Figure 4B**), patients with surgical bioprostheses having a labeled size ≤21 mm demonstrated significantly higher post-procedural mean gradients through 1 year (**Central Illustration**). Presence of total aortic regurgitation (AR) was infrequent following VIV, with 2.8% and 1.1% of patients experiencing moderate AR at discharge and 12 months, respectively. No patients had severe AR (**Figure 4C**). As such, the primary efficacy endpoint was met in 89 of 90 patients (98.9%) with evaluable mean gradient and AR data available at 12 months. One patient had a gradient >40 mm Hg (41 mm Hg), and no patients had AR greater than moderate. No statistically significant association between residual high discharge gradient and mortality was noted (Online Figure 2).

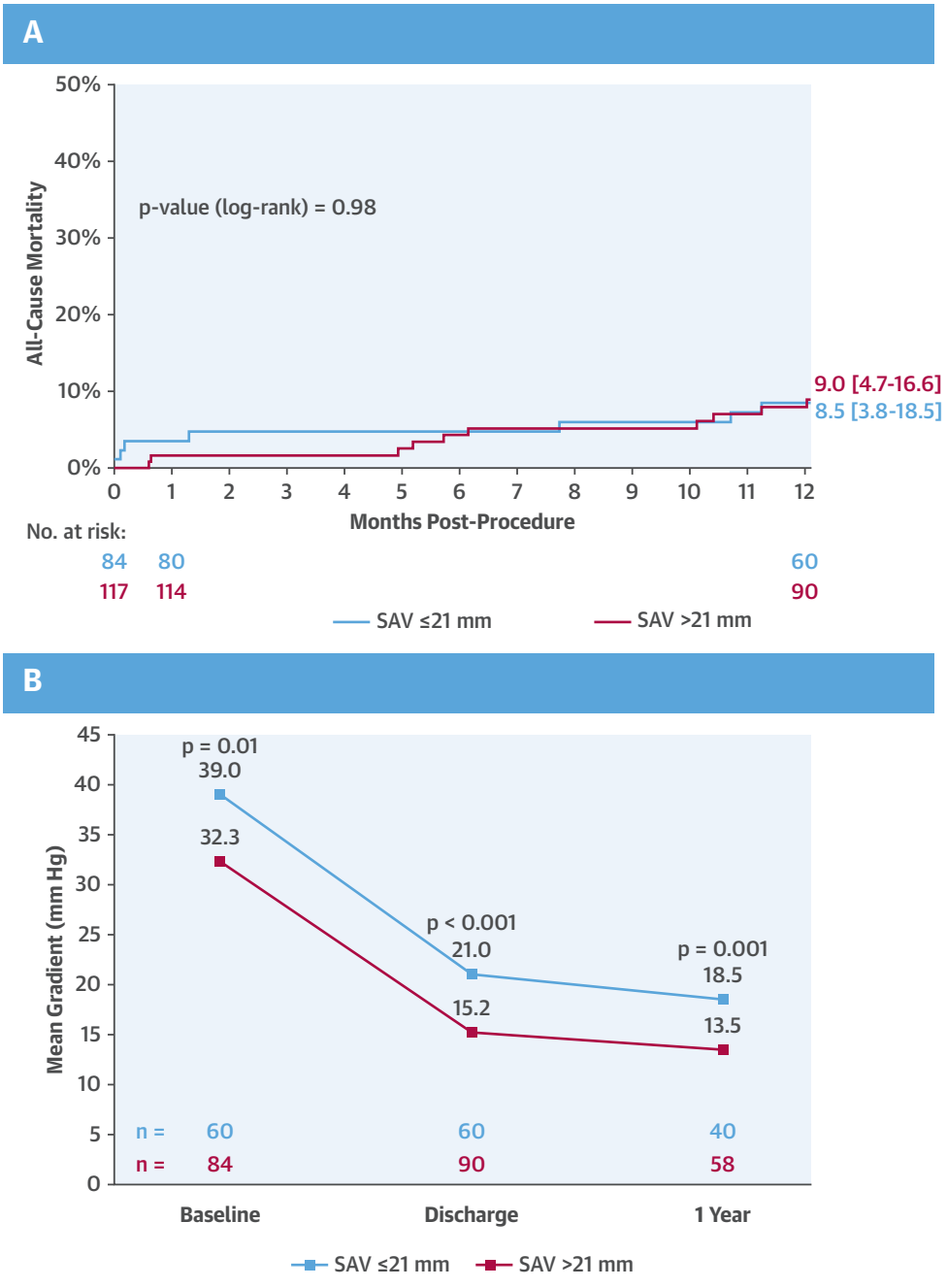
FUNCTIONAL STATUS. Improvements in functional status were noted through 12 months. Patients were commonly in New York Heart Association functional class III or IV at baseline (70.7%), but this had improved to only 10.3% of surviving patients in functional class III and 1.3% in functional class IV by 12 months (**Figure 5**). No differences in New York Heart Association functional class were noted when patients were stratified by the original size of their surgical bioprosthesis (Online Figure 3).

DISCUSSION

Early results from the VIVA trial confirm the consistent safety and efficacy results of performing catheter-based VIV interventions using the self-expanding CoreValve or Evolut R in failed surgical bioprostheses. One-year mortality was low (8.8% all cause, 5.6% cardiovascular), and rates of other clinical endpoints, including stroke, acute kidney injury, and new pacemaker implantation, were all relatively low and within acceptable ranges.

The 1-year all-cause mortality rate of 8.8% is the lowest reported among the 2 large prospective studies (CoreValve Expanded Use Study and PARTNER [Placement of Aortic Transcatheter Valve] II nested registry) and the retrospective VIVID (Valve-in-Valve International Data) registry (11–13). In contrast to the VIVID registry, which showed a significant

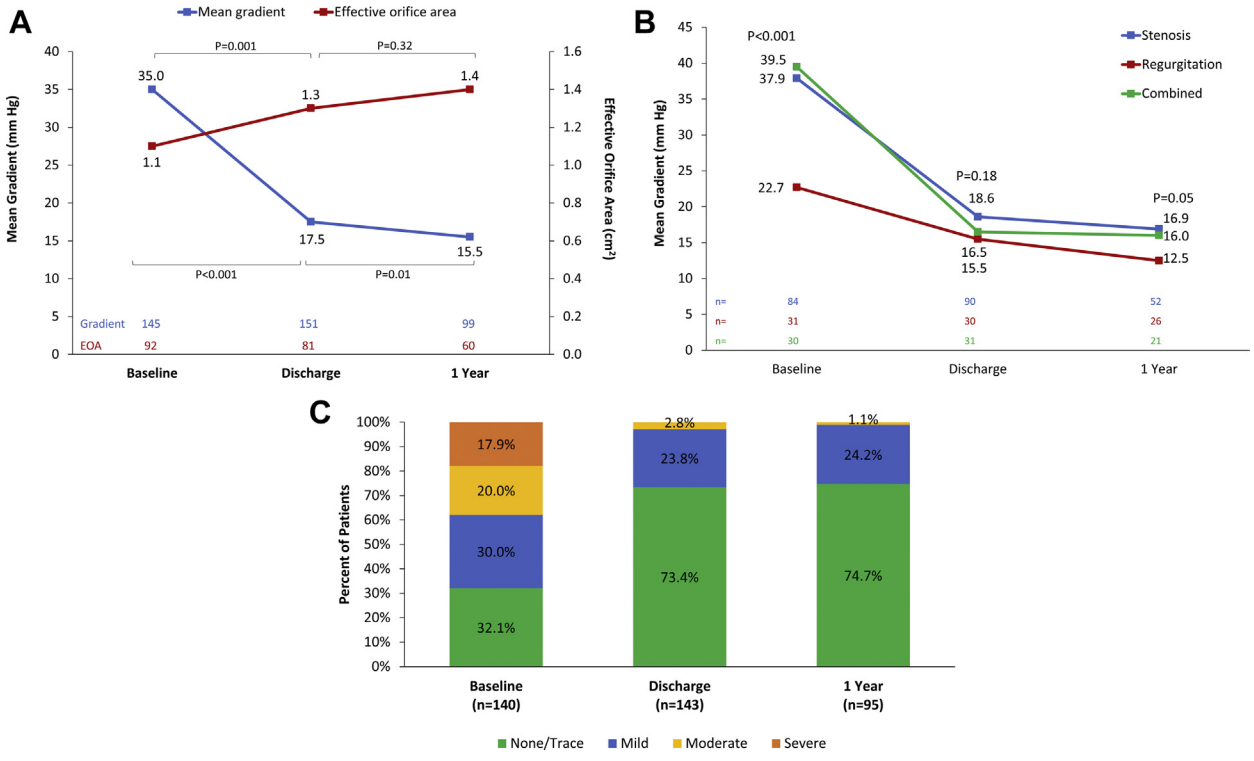
CENTRAL ILLUSTRATION **Clinical and Echocardiographic Outcomes According to Surgical Valve Size**



Tchétché, D. et al. J Am Coll Cardiol Intv. 2019;12(10):923-32.

(A) All-cause mortality by labeled size of the failed surgical valve. Rates are reported as Kaplan-Meier percentages (95% confidence intervals). **(B)** Mean gradient by surgical aortic valve (SAV) size, per independent echocardiographic core laboratory.

FIGURE 4 Valve Hemodynamic Status per Independent Echocardiographic Core Laboratory

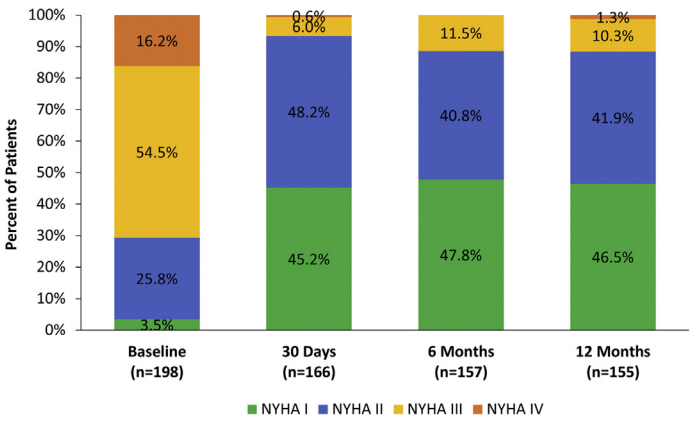


(A) Effective orifice area (EOA) and mean gradient in the overall cohort, **(B)** mean gradient by failure mode, and **(C)** total aortic regurgitation over time.

association between failure mode of the surgical valve and mortality, the present results failed to show a significant association, consistent with the findings of the CoreValve Expanded Use Study. However, it should be noted that at 30 days, all 5 deaths occurred in patients with stenosis as the mode of failure. Although several other VIV series have been reported previously, this trial is unique in that it is characterized by a large number of small-inner diameter surgical valves compared with valve sizes reported in other studies (11-13), as well as a large number of Mitroflow surgical valves. Both characteristics respectively expose patients to risk for high residual transprosthetic gradient and a high risk for coronary obstruction (11,17). This suggests that even with fewer comorbidities and a mean Society of Thoracic Surgeons score of 6.6%, VIVA comprised a complex patient population. Despite these challenges, excellent clinical results and hemodynamic status were achieved.

Mean aortic gradients were low at 1 year, despite disproportionately large numbers of surgical bioprostheses with labeled sizes ≤21 mm in this study (41.8%) and two-thirds of THVs used being CoreValve or Evolut R 23 mm devices. Importantly, mortality did not differ in patients with surgical bioprostheses ≤21 versus >21 mm, which is consistent with another recent VIV series (13). These findings demonstrate

FIGURE 5 New York Heart Association Functional Classification



New York Heart Association (NYHA) functional classification in the overall cohort. Deaths are excluded.

that even small-inner diameter surgical bioprostheses can be safely treated with this self-expanding platform. The supra-annular position of the CoreValve and Evolut R leaflets possibly explains the low gradients observed. Even if the inflow portion of the THV is constrained by the failed bioprosthesis, its leaflets, sutured 12 to 13 mm above, are more likely to function appropriately. Coronary artery obstructions are a major concern during and following VIV procedures, as they are associated with a high mortality rate (17–19). Five coronary obstructions occurred in this study: 3 during the procedure, 1 immediately following the procedure, and 1 that was identified several months later. All 4 procedural coronary obstructions occurred in patients with Mitroflow bioprostheses, in agreement with an analysis from the VIVID registry that showed the highest incidence of coronary obstruction in stented surgical bioprostheses with externally mounted leaflets (6.4%), followed by stentless (3.7%), and lowest in stented with internally mounted leaflets (0.7%) (17). Post-implantation balloon valvuloplasty was used in 20.8% of cases in VIVA (27.2% of stenosis cases), which may have aided in lowering gradients in some cases. This rate is higher than seen with a balloon-expandable device in the PARTNER II experience (13) (10.2%), but post-dilation rates were not reported in other larger VIV series for comparison. Emerging contemporary techniques, such as ring cracking using high-pressure balloons (to optimize post-valvular gradients) and leaflet slicing maneuvers (e.g., the BASILICA [bioprosthetic aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction] technique, to avoid left main coronary artery occlusion) were not used in the VIVA study. These emerging techniques need to be validated in prospective studies and/or large registries.

Malposition is also of concern with VIV. Only 6 patients (3.0%) in this series experienced procedural malpositioning of their THVs (4 patients had their valves retrieved, while 2 patients had ≥2 valves implanted). This is in contrast to 15.3% reported malpositioning in the VIVID registry (20) but similar to the 4 of 227 (1.8%) malposition rate reported in the CoreValve Expanded Use Study (12). Overall, the corrective repositioning feature of the Evolut R THV was used in 32 of 183 patients (17.5%). It represented a safety feature enabling more accurate positioning in complex situations.

STUDY LIMITATIONS. The VIVA trial has important limitations to consider. At the time of the study, there was no standardized practice to guide operators for how to best perform the VIV procedures. As such, procedural variables including post-dilation and implantation depth were left to operator discretion. Furthermore, implantation depth was not collected in this study, so further analysis cannot be conducted to evaluate outcomes related to this measure. Finally, this study had no formal statistical testing prespecified.

CONCLUSIONS

Early outcomes from the VIVA trial confirm the consistent safety and efficacy results of VIV interventions using a self-expanding CoreValve or Evolut R for failed surgical bioprostheses. Small-inner diameter surgical bioprostheses can be safely treated using this self-expanding platform.

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PERSPECTIVES

WHAT IS KNOWN? TAVR is a less-invasive alternative to redo surgical aortic valve replacement for patients who are at high surgical risk.

WHAT IS NEW? The VIVA trial is a real-world, prospective series of VIV data demonstrating excellent clinical and hemodynamic outcomes with self-expanding TAVR.

WHAT IS NEXT? Additional studies to evaluate VIV with newer generation devices along with emerging contemporary techniques are needed.

REFERENCES

1. Ruel M, Kulik A, Rubens FD, et al. Late incidence and determinants of reoperation in patients with prosthetic heart valves. Eur J Cardiothorac Surg 2004;25:364–70.

2. Jamieson WR, Burr LH, Miyagishima RT, et al. Re-operation for bioprosthetic aortic structural failure - risk assessment. Eur J Cardiothorac Surg 2003;24:873–8.

3. Kaneko T, Vassileva CM, Englum B, et al. Contemporary outcomes of repeat aortic valve replacement: a benchmark for transcatheter valve-in-valve procedures. Ann Thorac Surg 2015; 100:1298–304.

4. Maganti M, Rao V, Armstrong S, et al. Redo valvular surgery in elderly patients. Ann Thorac Surg 2009;87:521–5.

5. Popma JJ, Adams DH, Reardon MJ, et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. J Am Coll Cardiol 2014;63:1972–81.

6. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014; 370:1790–8.

7. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med 2017; 376:1321–31.

8. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–607.

9. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364: 2187–98.

10. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016; 374:1609–20.

11. Dvir D, Webb JG, Bleiziffer S, et al. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. JAMA 2014;312:162–70.

12. Deeb GM, Chetcuti SJ, Reardon MJ, et al. 1-Year results in patients undergoing transcatheter aortic valve replacement with failed surgical bioprostheses. J Am Coll Cardiol Intv 2017;10: 1034–44.

13. Webb JG, Mack MJ, White JM, et al. Transcatheter aortic valve implantation within degenerated aortic surgical bioprostheses: PARTNER 2 valve-in-valve registry. J Am Coll Cardiol 2017; 69:2253–62.

14. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. J Am Coll Cardiol 2012; 60:1438–54.

15. Oh JK, Little SH, Abdelmoneim SS, et al. Regression of paravalvular aortic regurgitation and remodeling of self-expanding transcatheter aortic valve: an observation from the CoreValve U.S. Pivotal Trial. J Am Coll Cardiol Img 2015;8: 1364–75.

16. Tchetche D, Van Mieghem NM. New-generation TAVI devices: description and specifications. EuroIntervention 2014;10 Suppl U: U90–100.

17. Ribeiro HB, Rodes-Cabau J, Blanke P, et al. Incidence, predictors, and clinical outcomes of coronary obstruction following transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: insights from the VIVID registry. Eur Heart J 2018;39: 687–95.

18. Dvir D, Leipsic J, Blanke P, et al. Coronary obstruction in transcatheter aortic valve-in-valve implantation: preprocedural evaluation, device selection, protection, and treatment. Circ Cardiovasc Interv 2015;8:e002079.

19. Jabbour RJ, Tanaka A, Finkelstein A, et al. Delayed coronary obstruction after transcatheter aortic valve replacement. J Am Coll Cardiol 2018; 71:1513–24.

20. Dvir D, Webb J, Brecker S, et al. Transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: results from the global valve-in-valve registry. Circulation 2012;126: 2335–44.

KEY WORDS aortic stenosis, self-expanding, TAVR, valve-in-valve

APPENDIX For a list of VIVA investigators as well as supplemental tables and figures, please see the online version of this paper.