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Original Article

Early and Midterm Clinical Outcomes of Transcatheter Valve-in-Valve Implantation Versus Redo Surgical Aortic Valve Replacement for Aortic Bioprosthetic Valve Degeneration: Two Faces of the Same Medal

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Objective: To compare early and midterm outcomes of transcatheter valve-in-valve implantation (ViV-TAVI) and redo surgical aortic valve replacement (re-SAVR) for aortic bioprosthetic valve degeneration.
Design: Patients who underwent ViV-TAVI and re-SAVR for aortic bioprosthetic valve degeneration between January 2010 and October 2018 were retrospectively analyzed. Mean follow-up was 3.0 years.
Setting: In-hospital, early, and mid-term outcomes.
Participants: Eighty-eight patients were included in the analysis.
Interventions: Thirty-one patients (37.3%) had ViV-TAVI, and 57 patients (62.7%) had re-SAVR.
Measurements and Main Results: In the ViV-TAVI group, patients were older (79.1 ± 7.4 *v* 67.2 ± 14.1, $p < 0.01$). The total operative time, intubation time, intensive care unit length of stay, total hospital length of stay, inotropes infusion, intubation >24 hours, total amount of chest tube losses, red blood cell transfusions, plasma transfusions, and reoperation for bleeding were significantly higher in the re-SAVR cohort ($p < 0.01$). There was no difference regarding in-hospital permanent pacemaker implantation (ViV-TAVI = 3.2% *v* re-SAVR = 8.8%, $p = 0.27$), patient-prosthesis mismatch (ViV-TAVI = 12 patients [mean 0.53 ± 0.07] and re-SAVR = ten patients [mean 0.56 ± 0.08], $p = 0.4$), stroke (ViV-TAVI = 3.2% *v* re-SAVR = 7%, $p = 0.43$), acute kidney injury (ViV-TAVI = 9.7% *v* re-SAVR = 15.8%, $p = 0.1$), and all-cause infections (ViV-TAVI = 0% *v* re-SAVR = 8.8%, $p = 0.02$), between the two groups. In-hospital mortality was 0% and 7% for ViV-TAVI and re-SAVR, respectively ($p = 0.08$). At three-years' follow-up, the incidence of pacemaker implantation was higher in the re-SAVR group (ViV-TAVI = 0 *v*

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re-SAVR = 13.4%, p < 0.01). There were no differences in reintervention (ViV-TAVI = 3.8% *v* re-SAVR = 0%, p = 0.32) and survival (ViV-TAVI = 83.9% *v* re-SAVR = 93%, p = 0.10) between the two cohorts.
Conclusions: ViV-TAVI is a safe, feasible, and reliable procedure.

Key Words: predictors of outcome; redo aortic surgery; TAVI valve-in-valve

SURGICAL AORTIC valve replacement (SAVR) with a bioprosthetic device remains the most frequently performed, gold standard method for treatment of severe aortic valve disease. The Achilles heel for bioprosthetic valves is the process of deterioration inherent to organic tissues exposed to repetitive stress. Patients who receive aortic bioprosthetic valves may experience valve degeneration requiring reoperation and replacement of the bioprosthesis.[1,2] Redo SAVR (re-SAVR) has been associated with an increased rate of mortality and complications such as stroke and pacemaker implantation, especially in the elderly population.[3,4] An alternative treatment approach is to implant a transcatheter aortic valve (TAVI) within the old bioprosthetic. Valve-in-valve TAVI (ViV-TAVI) has been associated with an increased rate of pacemaker (PM) implantation, especially in patients with small-size surgical valves. Moreover, the risk of obstructing the coronary ostium increases. Implantation techniques to mitigate such risks, including the BASILICA technique, the high implantation technique, and bioprosthetic valve fracture/remodeling, have shown good results.[5-10] However, there are other complications of ViV-TAVI that are not as easily mitigated. These include patient-prosthesis mismatch, paravalvular leak, the need for early reoperation, endocarditis, and acute kidney injury (AKI). Understanding all the risks of a new procedure is critically important because it allows surgeons to change or improve their practice based on objective criteria and, therefore, reduce patient harm from untested procedural "fads." Unfortunately, prospective clinical studies have not been done to compare ViV-TAVI versus re-SAVR, so the risks of this novel approach have not been weighed systematically against its proposed benefits.[12–16] The unique outcomes from this study included the type and brand of explanted valves and the postprocedural electrocardiographic changes when compared with other clinical studies. The authors sought to address this knowledge gap by investigating the early and midterm outcomes of a cohort of patients undergoing re-SAVR and ViV-TAVI at their institution, with a focus on the primary endpoints of freedom from death and stroke. The hypothesis of this study was that ViV-TAVI has a better risk-benefit profile compared with redo-SAVR.

Materials and Methods

Study Design

This was an observational cohort, single-center clinical study and data were collected from January 2010 to July 2018 in an institutional database. Patients undergoing ViV-TAVI and re-SAVR for failed bioprosthesis were included in the study. Patients with previous endocarditis, valve thrombosis, and mechanical aortic valve replacement were excluded (Fig 1).

Primary and Secondary Endpoints

The primary endpoints were freedom from death and stroke.[19] Secondary endpoints were patient-prosthesis mismatch, paravalvular leak, PM implantation rates, PR and QRS interval changes, reintervention, endocarditis, AKI[18], and New York Heart Association (NYHA) class at 30 days and at three years. With respect to in-hospital outcomes, the analyzed variables were intubation time, intubation >24 hours and intensive care unit (ICU) length of stay, inotropes usage, new atrial fibrillation, peak postoperative creatinine, reoperation for bleeding, transfusion rate, infection rate, chest tube losses, intra-aortic balloon pump (IABP) insertion, total hospital length of stay, on-table and in-hospital mortality, and NYHA class at hospital discharge. Early and midterm survival investigation was performed during checkups at the authors' hospital and additional phone calls during follow-up.

Statistical Analysis

Data were extracted manually from the database and analyzed using SPSS version 26 (SAS Institute, Cary, NC). Unpaired *t* test analysis was used for continuous variables, and Fisher's exact test analysis was used to test statistical significance for categorical variables. Continued variables are expressed as mean ± standard deviation. Freedom from mortality was calculated with Kaplan-Meier survival curves calculating the log-rank p value. In line with other clinical studies, a p value <0.01 was considered statistically significant. An age-adjusted Cox proportional hazard regression analysis was performed to calculate the survival rate in years. A Cox regression analysis was performed to assess the predictors of mortality at one year in the overall population. Demographic, clinical, and echocardiographic covariates were assessed singularly in the univariate analysis. Due to the retrospective nature of the study, patient consent was waived. For the follow-up analysis, patient phone consent was obtained. The follow-up data were acquired routinely during follow-up checkups at the authors' institution. Therefore, due to the retrospective nature of the study, there was

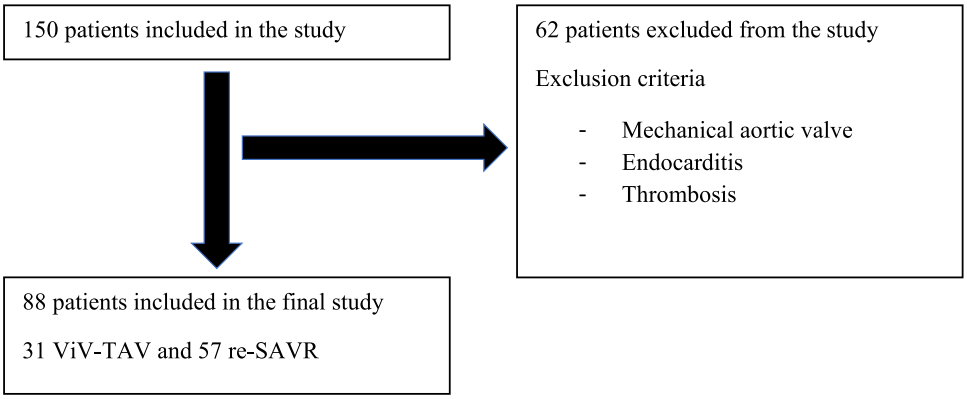

Fig 1. Flowchart study description. re-SAVR, redo surgical aortic valve replacement; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation.

no breach of confidentiality for the use of follow-up data. This study was authorized under 45 Ontario's Personal Health Information Protection Act, which does not require review by a research ethical board.

Clinical Data

Patient preoperative/postoperative data and complications were based on definitions set forth in the Society of Thoracic Surgeons' Adult Cardiac Database. Postoperative periprosthetic valve leakage entity was defined according to the American Heart Association guidelines.[17] In the ViV-TAVI group, patients with a previous TAVI procedure as their first surgery were included, and an unpaired *t* test was performed to compare the freedom from reoperation between the ViV-TAVI and re-SAVR groups. With respect to mortality, the authors included all deaths after valve implantation regardless of the cause. Early mortality was defined as mortality occurring during the first 30 days after the surgery.

Preoperative Evaluation

Preoperative diagnostic checkup screening included medication record, routine blood analysis, electrocardiogram, and echocardiography. On the electrocardiogram the authors recorded the PR and the QRS intervals in milliseconds. On the echocardiogram they recorded the ejection fraction, the left ventricular end-systolic diameters and volumes/end-diastolic diameters and volumes, the stroke volume (SV), the effective orifice area (EOA), the mean and maximum transvalvular gradients, the maximum transvalvular velocity, and the annular and aortic root diameters. In addition, the authors recorded the type, brand, and sizes of the valves. In patients undergoing the ViV-TAVI, a computed tomography scan TAVI gated with contrast was performed to assess the anatomy of the aortic valve, the aorta, and the femoral vessels to calculate the amount of calcium present in the valves and to perform a virtual transcatheter valve-to-coronary distance and estimated valve size. All patients underwent diagnostic coronary angiography.

Operative Data

Type of surgical access, cardioplegia solution total amount in milliliters, on-pump cardiac bypass time in minutes, aortic cross-clamp time in minutes, operating time in minutes, and IABP insertion were recorded.

Postoperative Evaluation

Patients had a postoperative electrocardiogram at ICU arrival and on postoperative days one and three. Postoperative echocardiography was performed in all the patients and the same preoperative data that were extracted were analyzed even in the postoperative control. Moreover, the authors recorded the postoperative incidences of prosthesis leakage and the patient-prosthesis mismatch.

Results

Patient Population

A total of 150 patients with a significant dysfunction of the aortic prosthesis were screened for inclusion in this analysis. After data collection, 27 patients with endocarditis, 30 patients with previous mechanical aortic valve prosthesis, and five patients with aortic valve thrombosis were excluded from the study. Ultimately, 88 patients were included in the analysis; of those, 31 (37.3%) underwent ViV-TAVI and 57 (62.7%) re-SAVR. Mean and maximum follow-up were three and 7.8 years, respectively. Baseline characteristics of these patients are shown in Table 1.

Patients in the ViV-TAVI group were significantly older (ViV-TAVI = 79.1 ± 7.4 *v* re-SAVR = 67.2 ± 14.1, $p < 0.01$), had lower weight in kilograms (ViV-TAVI = 73.7 ± 19.3 *v* re-SAVR = 77 ± 18.5, $p < 0.01$), and higher prevalence of coronary artery disease (ViV-TAVI = 80.6% *v* re-SAVR = 40.4%, $p < 0.01$) as well as preoperative use of diuretics (ViV-TAVI = 80.6% *v* re-SAVR = 46.4%, $p < 0.01$). Kidney function was significantly better in the re-SAVR group (creatinine clearance μmol/L [ViV-TAVI = 0.55 ± 0.31 *v* re-SAVR = 0.78 ± 0.34, $p < 0.01$]). More patients in the re-SAVR group were

Table 1
Baseline Patient Characteristics

Baseline Characteristics	ViV-TAVI (n = 31) (% SD)	re-SAVR (n = 57) (% SD)	*p* Value
Age, y	79.06 ± 7.4	67.19 ± 14.12	<0.01
>75 y	24 (mean 81.8 ± 3.72)	19 (mean 80.3 ± 3.4)	
Male sex	17 (54.8%)	29 (50.9%)	0.83
Weight, kg	73.7 ± 19.3	77 ± 18.5	<0.01
Height, m	1.63 ± 0.14	1.66 ± 0.1	0.1
BSA, m^2	1.8 ± 0.3	1.9 ± 0.3	0.97
BMI, kg/m^2	27.3 ± 4.9	27.7 ± 6.3	0.45
BMI >30	11 (mean 32.8 ± 2.6)	15 (mean 33.8 ± 2.7)	0.63
Euroscore II	9.46 ± 7.3	11.02 ± 9.33	0.42
NYHA			0.06
2	0	5 (8.8%)	
3	24 (77.4%)	47 (82.5%)	
4	7 (22.6%)	5 (8.8%)	
Hypertension	28 (90.3%)	47(82.5%)	0.49
Dyslipidemia	27 (87.1%)	42 (73.7%)	0.23
CAD	25 (80.6%)	23 (40.4%)	<0.01
LVEF %	49 ± 14.01	50.46 ± 12.84	0.62
Atrial fibrillation or flutter	12 (38.7%)	17 (29.8%)	0.54
Diabetes	7 (22.6%)	16 (28.1%)	0.79
Insulin treated	1 (3.2%)	0	0.75
Chronic obstructive pulmonary disease	5 (16.1%)	10 (17.5%)	1
Pre-operative creatinine, μmol/L	139.71 ± 107.67	112.21 ± 81.42	0.18
Creatinine clearance, μmol/L	0.55 ± 0.31	0.78 ± 0.34	<0.01
Stroke or TIA	5 (16.1%)	18 (31.6%)	0.18
Tobacco use or ex-smoker	7 (22.6%)	23 (40.4%)	0.14
ASA	29 (93.5%)	47 (82.5%)	0.26
β-blocker	14 (45.2%)	18 (32.1%)	0.16
ACE/ARB	20 (64.5%)	27 (48.2%)	0.14
Ca^2-antagonist	11 (35.5%)	13 (23.2%)	0.15
Statins	23 (74.2%)	31 (55.3%)	0.83
Diuretics	25 (80.6%)	26 (46.4%)	<0.01
PR interval msec	196.7 ± 36.4	181.7 ± 4	0.54
QRS interval msec	125.8 ± 37.9	122.3 ± 44.4	0.72
PM pre-operative	8 (25.8%)	5 (8.8%)	0.06
PVD	16 (51.6%)	22 (38.6%)	0.34
Elective surgery	31(100%)	39 (68.4%)	<0.01
STEMI <90 d	1 (3.2%)	2 (3.5%)	1
Platelet count E9/L	176.5 ± 65.4	193 ± 60.5	0.23
Warfarin therapy	5 (16.1%)	10 (17.5%)	1
INR	1.19 ± 0.20	1.22 ± 0.39	0.68
Primary operative combined	13 (41.9%)	25 (43.9%)	1
Size of explanted valves	23.9 ± 2	23.4 ± 2.5	0.38
Aortic stenosis	14 (45.16%)	31 (54.4%)	0.54
Primary bicuspid valve	3 (13.04%)	22 (39.3%)	0.03
Previous associated surgical procedures			
CABG	10 (32.3%)	10 (17.5%)	0.19
Mitral valve surgery	1(3.2%)	6 (10.5%)	0.42
Tricuspid valve surgery	0	1 (1.8%)	1
Aortic arch surgery	3 (9.7%)	7 (12.3%)	0.98
Bentall procedure	1 (3.2%)	2 (3.5%)	1
Pre-operative echocardiographic data			
EOA, cm^2	1.22 ± 0.58	1.01 ± 0.51	0.08
Peak gradient, mmHg	48 ± 26.4	65.5 ± 32.1	0.01
Mean gradient, mmHg	29.6 ± 18.4	39.5 ± 20.3	0.02
Vmax, m/s	3.2 ± 1.2	3.8 ± 1	0.02
Root diameter, cm	3.4 ± 0.4	3.4 ± 0.5	0.71
Annulus diameter, cm	2.1 ± 0.2	2.1 ± 0.3	0.99
LVEDd, mm	5.1 ± 0.7	5.1 ± 0.8	0.90
LVESd, mm	3.7 ± 0.8	3.6 ± 0.9	0.64
LVEDV, mL	148.35 ± 51.2	136.5 ± 57.1	0.40
LVESV, mL	66.2 ± 51.6	52.8 ± 37.9	0.23
SV, mL/s	86.5 ± 28.2	81.2 ± 25.8	0.4

Abbreviations: ACE, angiotensin-converting enzyme; ARB, Angiotensin II Receptor Blockers; ASA, American Society of Anesthesiologists; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass surgery; CAD, coronary artery disease; EOA, effective orifice area; INR, international normalized ratio; LVEDd, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESd, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; NYHA, New York Heart Association; PM, pacemaker; PR, ECG waves; PVD, peripheral vascular disease; QRS, ECG waves; re-SAVR, redo surgical aortic valve replacement; STEMI, ST-elevation myocardial infarction; SV, stroke volume; TIA, transient ischemic attack; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation; Vmax, maximum veloxity.

done as an urgent intervention (ViV-TAVI = 0% *v* re-SAVR = 31.6%, p < 0.01). The definition of urgent intervention was based on AHA guidelines. Preoperative electrocardiogram and echocardiography data are provided in Table 1.

There were no differences between the groups in terms of PR interval duration in msec and QRS interval duration in msec. An equivalent number of patients in each cohort underwent intervention for aortic prosthetic valve stenosis (ViV-TAVI = 45.16% *v* re-SAVR = 54.4%, p = 0.5), and excluded cases were prosthetic valve regurgitation and mixed cases. Intraoperative outcomes are summarized in Table 2.

During the perioperative period, the re-SAVR group had a higher operative time in minutes (ViV-TAVI = 85.1 ± 24.8 *v* re-SAVR = 251.2 ± 80.7, p < 0.01). The average cardiopulmonary bypass time and aortic cross-clamp times for re-SAVR were 109.9 ± 40.9 and 88.3 ± 34.4. Associated surgical procedures in the re-SAVR group were CABG in seven patients, mitral valve surgery in seven patients (four valve repair and three valve replacement), ascending aortic surgery in nine patients, and pulmonary artery repair in one patient. In the ViV-TAVI group the most performed surgical access was transfemoral access in 26 patients (83.13%), followed by transapical access in three patients (9.67%), and the transaortic and axillary accesses had one patient each with 3.2%, respectively. In-hospital postoperative variables are summarized in Table 3.

Postoperative intubation time in hours (ViV-TAVI = 1.3 ± 1.9 *v* re-SAVR = 34.33 ± 72.11, p < 0.01) was higher in the re-SAVR group, despite the lack of significant preoperative differences in the incidence of Chronic Obstructive Pulmonary Disease (COPD) between the two groups. In addition, ICU length of stay in hours (ViV-TAVI = 18.17 ± 5.87 *v* re-SAVR = 79.3 ± 113.56, p < 0.01), total hospital length of stay in days (ViV-TAVI = 3.6 ± 3.23 *v* re-SAVR = 10.16 ± 8.31, p < 0.01), inotropes infusion (ViV-TAVI = 41.93% *v* re-SAVR = 94.73%, p < 0.01), intubation >24 hours (ViV-TAVI = 0% *v* re-SAVR=

Table 2
Intraoperative and Echocardiographic Data

Intraoperative and Echocardiographic Data	ViV-TAVI (n = 31) (% SD)	re-SAVR (n = 57) (% SD)	*p* Value
Cardioplegia volume, mL	0	5,084.2 ± 2,655.1	
CPB time, min	0	109.9 ± 40.9	
Aortic clamp, min	0	88.3 ± 34.4	
OR time, min	85 ± 24.8	251.2 ± 80.7	<0.01
IABP intra-operative	0	1 (1.8%)	1
Femoral access	26 (83.13%)	3 (5.2%)	<0.01
Transapical access	3 (9.67%)	0	0.01
Transaortic access	1 (3.2%)	0	0.75
Axillary access	1 (3.2%)	2 (3.5%)	1
Size of valves	24.1 ± 2.4	22.5 ± 6.5	
Size 19-21	2	28	
Size 23-25	20	22	
Size ≤25	9	7	
Combined second surgery	0	30 (52.6%)	
Associated CABG surgery	0	7	
Associated mitral surgery	0	7	
Associated ascending aorta/root surgery	0	9/6	
PR interval msec	186.7 ± 41.4	188.5 (± 38.9)	0.8
QRS interval msec	125.8 ± 37.9	121.8 (± 36.6)	0.6
LVEDd, mm	4.8 ± 0.7	4.7 ± 0.6	0.32
LVESd, mm	3.4 ± 0.9	3.3 ± 0.7	0.39
LVEDV, mL	123.3 ± 61	117.5 ± 54.3	0.67
LVESV, mL	51.2 ± 42.4	48 ± 34.9	0.72
SV (LVOT) mL/s	74.2 ± 25.5	67.2 ± 21.1	0.18
EOA, cm^2	1.35 ± 0.38	1.58 ± 0.48	0.02
iEOA, cm^2/m^2	0.76 ± 0.29	0.84 ± 0.25	0.16
iEOA <0.65 cm^2/m^2	12 (mean 0.53 ± 0.07)	10 (mean 0.56 ± 0.08)	0.4
Vmax, m/s	2.4 ± 0.8	2.5 ± 0.6	0.57
Mean gradient, mmHg	16.8 ± 1	16.2 ± 7.2	0.72
EF %	45 ± 14.4	47.1 ± 15	0.42
Postoperative regurgitation	15 (48.4%)	0	<0.01
Leak mild/moderate/severe	14 mild/1 moderate	0	

Abbreviations: CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; EF, ejection fraction; EOA, effective orifice area; IABP, intraaortic balloon pump; iEOA, indexed effective orifice area; LVEDd, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVESd, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; LVOT, left ventricular outflow tract; OR, operating room; re-SAVR, redo surgical aortic valve replacement; SV, stroke volume; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation; Vmax, maximum velocity.

19.3%, p < 0.01), reoperation for bleeding (ViV-TAVI = 0% *v* re-SAVR = 15.8%, p < 0.01), chest tube loss in mL (ViV-TAVI = 68.7 ± 360 *v* re-SAVR = 624.7 ± 597, p < 0.01), red blood cell transfusion in units (ViV-TAVI = 0.19 ± 0.47 *v* re-SAVR = 2.63 ± 2.73, p < 0.01), platelets transfusion in units (ViV-TAVI = 0 *v* re-SAVR = 0.72 ± 1.1, p < 0.01), and atrial fibrillation incidence (ViV-TAVI = 9.7% *v* re-SAVR = 47.4%, p < 0.01) were higher in the re-SAVR group. Mild periprosthetic valve leakage was more frequent in the ViV-TAVI group (ViV-TAVI = 48.4% *v* re-SAVR = 0%, p < 0.01) (Table 2). Dialysis was required for three patients in the ViV-TAVI group and nine patients in the re-SAVR group. There were five episodes of infections in the surgical group, with four episodes of lung infections and one episode of urinary tract infection. There was no sternal wound infection norleg wound infection event.

Table 3
In-Hospital and Midterm Outcomes

In-Hospital Outcomes	ViV-TAVI (n = 31) (% SD)	re-SAVR (n = 57) (% SD)	*p* Value
Intubation time hours	1.3 ± 1.9	34.33 ± 72.11	<0.01
ICU, h	18.17 ± 5.9	79.3 ± 113.6	<0.01
Total hospital length of stay, d	3.6 ± 3.2	10.2 ± 8.3	<0.01
Re-intubation	0	5 (8.8%)	0.02
Readmission in ICU	0	3 (5.3%)	0.49
Inotropes	13 (41.93%)	54 (94.73%)	<0.01
Mild	12 (38.7%)	23 (40.4%)	
Moderate	0	18 (31.6%)	
Severe	1 (3.2%)	15 (26.3%)	
Norepinephrine	12 (38.7%)	56 (98.2%)	<0.01
Epinephrine	0	11 (19.3%)	<0.01
Dobutamine	5 (16.1%)	29 (50.9%)	<0.01
Milrinone	0	7 (12.3%)	<0.01
AKI	3 (9.7%)	9 (15.8%)	0.1
Atrial fibrillation	3 (9.7%)	27 (47.4%)	<0.01
Intubation >24 h	0	11 (19.3%)	<0.01
Stroke or TIA	1 (3.22%)	4 (7%)	0.43
New PM implant	1 (3.22%)	5 (8.8%)	0.27
Reoperation for bleeding	0	9 (15.8%)	<0.01
Infection	0	5 (8.8%)	0.02
Type of infection	0	3 Klebsiella	
		1 Serratia	
		1 Routella	
On-table mortality	0	1 (1.75%)	
Hospital mortality	0	4 (7%)	0.08
Peak postoperative creatinine, μmol/L	129.07 ± 87.67	111.26 ± 89.05	0.41
Chest tubes loss, mL	68.7 ± 359.2	624.6 ± 596.6	<0.01
RBC transfusion units	0.19 ± 0.47	2.63 ± 2.73	<0.01
Platelets transfusion units	0	0.72 ± 1.1	<0.01
Plasma transfusion units	0	1.22 ± 2	0.03
IABP	0	0	
Alive at discharge	31 (100%)	52 (93%)	
Midterm Outcomes			
Alive	26 (83.9%)	52 (93%)	0.1
PM implantation	0	7 (13.4%)	<0.01
Endocarditis	0	0	0
Reintervention	1 (3.8%)	0	0.32
Stroke	1 (3.8%)	4 (7.7%)	0.41
AKI	3 (11.5%)	4 (7.7%)	0.7
NYHA			0.7
1	6 (23.07%)	10 (19.23%)	
2	13 (50%)	22 (42.3%)	
3	7 (26.92%)	9 (17.3%)	
4	0	4 (7.69%)	
Type of Prosthesis			
Explanted Valves			
Edwards Sapien	6	0	
Carpentier Edwards	4	15	
Toronto Freestyle Stentless	4	5	
Hancock 2	2	0	
Mitroflow	10	28	
St. Jude Portico	1	0	
Triflecta	3	2	
Medtronic Ultra Porcine (Mosaic)	1	0	
Tissue unknown type	0	7	
Implanted Valves			
Corevalve evolute	9	0	
Edwards Sapien	6	0	
Edwards Sapien 3	4	0	
Edwards Sapien XT	7	0	

(*continued*)

Table 3 (*continued*)

In-Hospital Outcomes	ViV-TAVI (n = 31) (% SD)	re-SAVR (n = 57) (% SD)	*p* Value
St. Jude Portico	5	0	
Carbomedics Mechanical	0	7	
Magna ease	0	19	
Mitroflow	0	7	
Perceval	0	12	
St. Jude Mechanical	0	9	
Triflecta	0	3	

NOTE. Mild, one inotrope; moderate, two inotropes; severe, more than three inotropes.
Abbreviations: AKI, acute kidney injury; IABP, intraaortic balloon pump insertion; ICU, intensive care unit; NYHA, New York Heart Association; PM, pacemaker; RBC, red blood cells; re-SAVR, redo surgical aortic valve replacement; TIA, transitory ischemic attack; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation.

There was only one on-table mortality in the re-SAVR group, and in-hospital mortality was 0% and 7% for ViV-TAVI and re-SAVR, respectively (p = 0.08). Primary endpoints also were stratified by EuroScore II Risk of Mortality >5% in both cohorts (Table 4). Using this stratification scheme, the authors did not find a significant difference between the ViV-TAVI and re-SAVR groups. Postoperative electrocardiogram and echocardiographic data are summarized in Table 3.

The postoperative echocardiographic data did not show a statistically significant difference between the groups. There was no difference between the groups regarding the indexed effective orifice area (iEOA) in cm^2/m^2, and a subgroup analyses of severe patient-prosthesis mismatch (iEOA <0.65 cm^2/m^2) also did not show any differences. Explanted and implanted bioprostheses are summarized in Table 3.

The Mitroflow bioprosthesis was the most explanted valve (28 patients), and the Perceval was one of the most implanted valves. The authors did not collect data on the total number of Mitroflow bioprostheses implanted during the study timeframe. There was no difference in terms of timing of reintervention in years between the groups. In addition, no difference regarding freedom from reintervention between the two cohorts was found (Fig 2).

Table 4
Primary and Secondary Endpoints Stratified by Euroscore II Risk of Mortality >5% in Both Cohorts

	ViV-TAVI (n = 26) (SD %)	re-SAVR (n = 40) (SD %)	*p* Value
Euroscore II >5%	10.52 ± 7.5	14.17 ± 9.5	0.13
Survival at hospital discharge	26 (100%)	37 (92.5%)	0.15
iEOA, cm^2/m^2	0.77 ± 0.31	0.83 ± 0.27	0.27
Stroke or TIA	1 (3.8%)	3 (7.5%)	0.5
Mild paravalvular leak	10 (38.46%)	0	0.34

Abbreviations: iEOA, indexed effective orifice area; re-SAVR, redo surgical aortic valve replacement; TIA, transitory ischemic attack; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation.

Follow-Up

Primary Endpoints

At three years, there was no difference between the groups in terms of survival (Table 3), as demonstrated in the Kaplan-Meier survival curve and the age-adjusted Cox proportional hazard regression analysis (Fig. 3A, 3B). In the univariate and multivariate Cox regression analyses (Table 5), the only predictive factor for mortality at three years was a larger body mass index (BMI), hazard ratio 1.1; 95% CI, 1.03-1.29; p < 0.01, and hazard ratio 1.18; 95% CI, 1.04-1.34, respectively (Table 5). It is possible that BMI was merely a surrogate marker for surgical technique because those in the surgical AVR group had a significantly larger BMI and trend toward higher mortality than the ViV-TAVI group.

Secondary Endpoints

The incidence of PM implantation in the re-SAVR group was higher (ViV-TAVI = 0 *v* re-SAVR = 13.4%, p < 0.01). There were no differences in reintervention, endocarditis, and AKI. Regarding the NYHA class, there was no difference between the outcomes of the two cohorts (p = 0.7). Prevalence of NYHA I, II, III, and IV was similar between the groups (Table 3). Only one ViV-TAVI patient underwent aortic valve bioprosthesis implantation at two years following the transcatheter procedure due to severe paravalvular leakage. There were no reinterventions in the surgical group.

Discussion

This retrospective analysis found that ViV-TAVI had comparable early and midterm outcomes to re-SAVR. In addition, the authors performed an ECG analysis and type of explanted valves. The main findings from this study can be summarized as follows. First, ViV-TAVI was not inferior to re-SAVR with respect to the primary endpoints at three years' follow-up (freedom from death and stroke). The 7% mortality rate can be attributed to the urgency of the surgeries and was closely related to the predicted EuroScore II, with 11.8% of estimated risk of complications including death. One of the most recent papers, by Tam et al,[11] with 262 patients, reported a late mortality of 33.2% in the redo SAVR group and 23.2% in the ViV-TAVI group. On the other hand, Grubitzsch et al[25] reported an early mortality of 8% in the redo SAVR and 11% in the ViV-TAVI group, respectively. A 7% mortality is in line with the actual literature. With respect to the outcomes, almost 30% of the patients in the redo SAVR group and 38.7% in the ViV-TAVI group had atrial fibrillation/flutter. As the authors know, this is one of the major risk factors for stroke. In addition, diabetes (28.1%), previous stroke or transitory ischemic attack (31.6%), and tobacco use (40.4%) have affected this outcome. Silachi et al[26] and Grubitzsch et al[25] in the redo SAVR group reported 4% of disabling stroke in the early outcomes. On the other hand, Eijofor et al[28] reported 9.1% of stroke in the early outcomes.

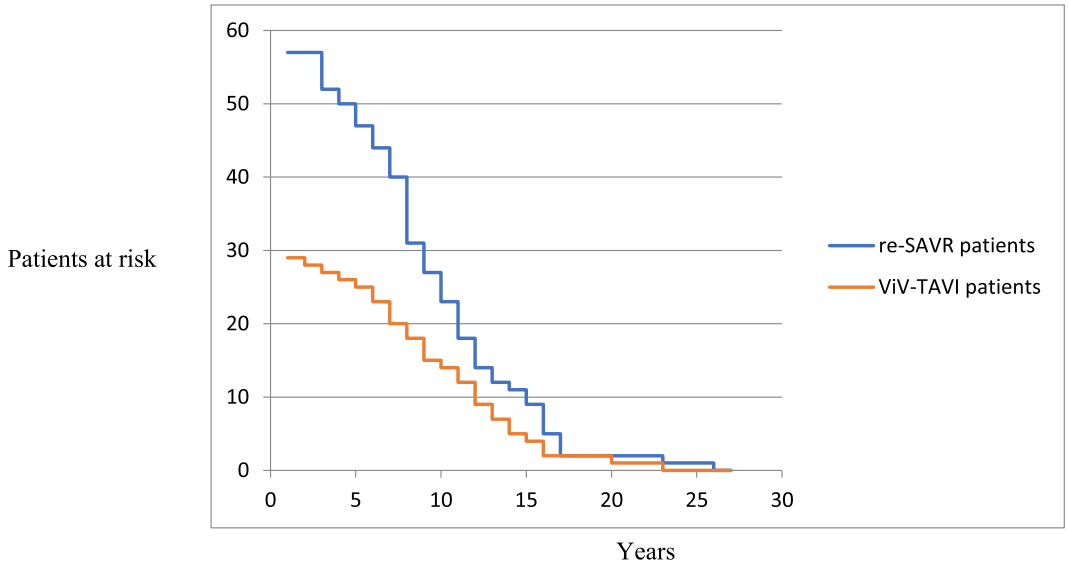

Fig 2. Analysis of freedom from reintervention. re-SAVR, redo surgical aortic valve replacement; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation.

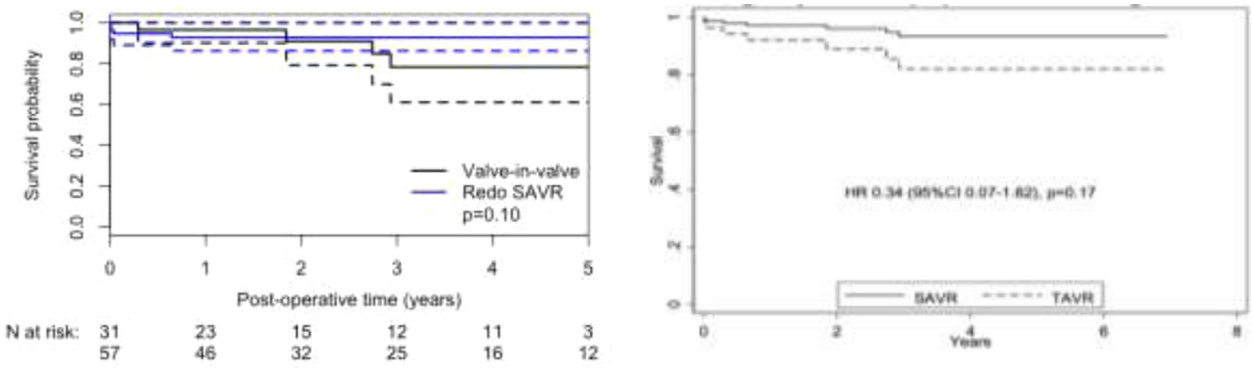

Fig 3. Kaplan-Meier survival curve and age-adjusted Cox proportional regression analysis. SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

Therefore, a 7% stroke risk is in line with results from the international literature. Moreover, the authors used cerebral oximetry during surgery to monitor cerebral malperfusion. Second, with respect to patient-prosthesis mismatch, the study did not find any difference between the groups. Similar to other clinical studies, the authors performed an analysis of the time to degeneration of the prosthesis. Third, several benefits of the secondary endpoints were associated with ViV-TAVI regarding in-hospital outcomes including decreased ICU and hospital lengths of stay, lower risk of bleeding/transfusion rate, lower dosage of inotropic support, lower incidence of atrial fibrillation, and intubation >24 hours. The high reoperative bleeding rate in this series may have been related to the surgeons' experience. Some of the surgeries were performed by nonsenior surgeons and 18% of patients were on warfarin therapy. At follow-up, the ViV-TAVI had a lower incidence of PM implantation. The findings of noninferiority of ViV-TAVI compared with re-SAVR were robust and in line with other clinical studies.[20-29] Fourth, there was no difference between the two groups with respect to the number of patients who experienced a stroke. This may be attributed to the intraprocedural surgeon experience, accurate and early treatment of new onset of arrhythmias, and technologic improvements and profiles of the prosthesis. Fifth, the Mitroflow bioprosthesis was found to be the most explanted valve (28 patients), which led the authors to decrease the frequency at which this valve was implanted in their patients. Conversely, the Perceval valve was one of the most implanted valves and elicited good postoperative results. In addition, prosthetic mismatch showed no difference. The metanalysis by Nalluri et al showed no difference in mean postprocedural gradients.[11,33] Sixth, the authors did not find any significant differences in the length of PR and QRS interval changes, suggesting that the risk for complete heart block was similar. With respect to the risk factors before surgery, the drivers for high-risk redo SAVR included several factors such as the high rate of urgent surgeries (32%) and the high EuroScore II in the re-SAVR group. Grubitzsch et al[25] found that age, EuroScore II, pulmonary hypertension, renal failure, patent left internal mammary artery (LIMA) graft, and

Table 5
Multivariate Cox Regression Analysis

Covariate	Hazard Ratio (95% Confidence Interval)	*p* Value
Male sex	78 (0.20-1.000)	>0.01
Body mass index	1.1 (1.03-1.29)	<0.01
Euroscore II	1.07 (1.00-1.14)	>0.01
NYHA class	0.8 (0.10-6.0)	>0.01
Hypertension	25 (0.01-1.000)	>0.01
Dyslipidemia	29 (0.01-1.000)	>0.01
Coronary artery disease	0.85 (0.12-6.1)	>0.01
Atrial fibrillation or flutter	1.91 (0.27-13.4)	>0.01
Diabetes	0.95 (0.1-9.2)	>0.01
Chronic obstructive pulmonary disease	2,080(0.01-1.000)	>0.01
Creatinine level	0.99 (0.96-1.02)	>0.01
Tobacco use (active or past)	0.52 (0.07-3.7)	>0.01
Valve prosthesis size	0.8 (0.5-1.3)	>0.01
Paravalvular leak postoperative	28 (0.01-1.000)	>0.01
ViV-TAVI	40 (0.01-1.000)	>0.01
Left ventricular ejection fraction	0.92 (0.86-1.0)	>0.01
LVEDd pre-operative	0.71 (0.29-1.74)	>0.01
LVESd pre-operative	0.54 (0.14-2.0)	>0.01
Max aortic velocity postoperative	1.33 (0.34-5.2)	>0.01

Abbreviations: LVEDd, left ventricular end-diastolic diameter; LVESd, left ventricular end-systolic diameter; NYHA, New York Heart Association; ViV-TAVI, valve-in-valve transcatheter aortic valve implantation.

concomitant surgical procedure are the most important criteria for decision-making. On the other hand, the drivers that influenced the early outcomes from the same group in the univariate analysis were: (1) more than one concomitant procedure, (2) coronary obstruction, (3) life-threatening bleeding, (4) mechanical circulatory support, and (5) inotropes >48 hours. In the authors' univariate analysis, they found the same drivers with the addition of atrial fibrillation, ICU, and total hospital length of stay and chest tubes loss with correlated blood products transfusions. However, due to the small number of patients, the multivariate analysis found that BMI was the only preoperative significant factor. To the best of the authors' knowledge, this was one of the largest single-center studies in the literature that compared the echocardiographic and surgical outcomes of ViV-TAVI versus re-SAVR, and had one of the longest follow-ups with primary and secondary endpoints of survival rate, stroke, patient-prosthesis mismatch, and paravalvular leakage. With respect to the TAVI implantation height, the authors did not experience a significant association between these patients and those who had a postoperative myocardial infarction. Primary and secondary endpoints with a Euroscore II >5% did not show any significant changes between the two groups. In line with other clinical studies, the authors included in the re-SAVR group patients who had undergone additional surgical procedures[30,33] and in the VIV-TAVI group those who had undergone a previous TAVI. The outcomes of the study potentially could help to identify the patients who may benefit from experienced TAVI centers. Moreover, Medicare recently has revised its national coverage determination for TAVI[31], and a study by Hechuan et al[32] found that the number of cardiac surgical hospitals providing TAVI could double under the new surgical volume requirements. In this study, >50% of the surgical cases included concomitant surgical procedures. As a result, the extent to which the findings can be generalized is hindered.

Study Limitations

This was an observational, retrospective, single-center clinical study and possessed an inherent bias associated with its design. As expected, patients in the ViV-TAVI group had increased age, weight, and CAD incidence. On the other hand, due to the nature of the nonurgent ViV-TAVI procedures, there were more cases of urgent surgery in the re-SAVR group. The lack of matching and randomization to treatment groups was a severe limitation. In addition, the power of this retrospective study was lower than that of a propensity-matched clinical study. Moreover, the lack of data in both the pre- and postoperative periods posed a challenge to the interpretation of the associated outcomes. Due to the nature of the TAVR procedure (urgent TAVRs are rare), comparing this population with the redo-SAVR one (in which urgent cases are included) may be biased. However, in line with other clinical studies that compared ViV-TAVR versus redo-SAVR, the authors did not exclude the urgent cases from the redo-SAVR group. The Society of Thoracic Surgeons' score includes multiple cofactors such as illicit drug use, alcohol use, etc, which were not present in the authors' database. Therefore, they used the EuroScore II as a predictive risk score. However, the EuroScore II measures risk of cardiac surgery, not of TAVR. Moreover, the authors acknowledge that comparing cardiac surgical procedures and ViV-TAVI may have introduced bias. Furthermore, >50% of the surgical cases included other surgeries, which made the comparison of these secondary outcomes unsurprising. The authors did not perform an in-hospital analysis of nonconcomitant procedures in redo-SAVR versus ViV-TAVI due to the small number of patients. They also did not report a patient frailty index because it was not recorded in the data. Confounding variables, such as patient ethnicity (which was not recorded in the data), may have affected patient complications and survival rates. The size of the patient population also posed an additional limitation, as only 88 patients were included in this study. As a result, the extent to which the findings can be generalized was hindered. Cardiac surgery is a learning process and during those difficult redo-SAVR procedures, most of the time the young surgeon was mentored from a senior colleague. Therefore, data of the patients operated on by these surgeons were included in the analysis. The patients who experienced a myocardial infarction lacked original electrocardiogram tracings at the time of the study; therefore, myocardial infarction outcomes were not included in the analysis. Multiinstitutional studies that are performed during a long postoperative period on a larger patient population should be conducted to further validate the findings from this investigation.

Conclusions

This study found that ViV-TAVI is a safe, feasible, and reliable procedure. This is supported from the primary and secondary endpoint outcomes obtained from the two cohorts.

Conflict of Interest

None.

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