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Valve-in-Valve Transcatheter Aortic Valve Implantation for Degenerated Bioprosthetic Heart Valves

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Objectives We sought to analyze outcomes of patients with degenerated surgically implanted bioprosthetic heart valves undergoing valve-in-valve (viv) transcatheter aortic valve implantation (TAVI).

Background Redo cardiac surgery for degenerated bioprosthetic heart valves is associated with increased risks, particular in elderly patients with comorbidities. For these patients, TAVI may be an attractive, less invasive treatment option.

Methods Data from 47 patients age 64 to 97 years (logistic euroSCORE: 35.0 ± 18.5%) undergoing transfemoral (n = 25) or transapical (n = 22) viv-TAVI for failed bioprosthetic aortic valves 113 ± 65 months after initial surgery at 9 clinical sites in Germany and Switzerland were analyzed.

Results Valve-in-valve TAVI was technically successful in all patients, with 2 patients requiring bail-out implantation of a second TAVI prosthesis for severe regurgitation during the procedure. There was 1 procedural death as the result of low-output failure. Valvular function after viv-TAVI was excellent with respect to valve competence, but increased transvalvular gradients ≥20 mm Hg were noted in 44% of patients. Vascular access complications occurred in 6 (13%) patients, and 5 (11%) patients required new pacemaker implantation after viv-TAVI. Renal failure requiring dialysis occurred in 4 (9%) patients. Mortality at 30 days was 17% (1 procedural and 7 post-procedural deaths), with 3 of 8 fatalities the result of non–valve-related septic complications.

Conclusions Valve-in-valve TAVI can be performed with high technical success rates, acceptable post-procedural valvular function, and excellent functional improvement. However, in these predominantly elderly high-risk patients with multiple comorbidities, viv-TAVI was associated with 17% mortality, often because of septic complications arising in the post-operative phase. (J Am Coll Cardiol Intv 2011;4:1218–27) © 2011 by the American College of Cardiology Foundation

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Transcatheter aortic valve implantation (TAVI) has emerged to become an attractive, less invasive treatment option for patients with symptomatic severe aortic valve stenosis (1,2). Currently, patients deemed at excessive risk for conventional surgical valve replacement are considered candidates for TAVI (3). These patients are typically elderly patients with significant comorbidities, usually reflected by a logistic euroSCORE of >20% or a Society of Thoracic Surgeons (STS) risk of mortality of >10% for perioperative mortality (4). Patients with other factors that increase surgical risk but that are not captured by these scoring systems (e.g., general frailty, porcelain aorta, prior chest radiation, or cardiac surgery) are also deemed appropriate candidates for TAVI (5,6). In particular, patients with degeneration of previously surgically implanted tissue heart valves may potentially benefit from beating-heart TAVI, obviating the risks associated with using cardioplegia and cardiopulmonary bypass during redo surgery (7).

Previous animal studies and selected case series have suggested that valve-in-valve (viv) TAVI for degenerated surgical bioprostheses is technically feasible and safe (8–15). However, the small number of patients undergoing viv-TAVI reported so far even at pioneering centers precludes reliable insights into the clinical success and complication rates of viv-TAVI (11,12,14). The major goal of this study was to provide insights into the technical success and outcomes in patients undergoing viv-TAVI in contemporary practice across several clinical sites in Germany and Switzerland.

Methods

Registry design. The present independent registry on viv-TAVI was founded by an interdisciplinary group of TAVI experts (H.E., U.S., H.T., H.B., P.K., M.T., T.W.). The rarity of patients undergoing viv-TAVI at the present time precludes larger numbers of cases with this particular TAVI indication even at a very large tertiary care single center. Our registry was designed to collect data on this specific TAVI indication across several referral sites to accumulate a maximum of information on a larger number of cases with this otherwise rare condition with the hope of providing extended insights into clinical success and complication rates. The registry was approved by the ethics committee of the University of Duisburg–Essen. There was no funding by the industry.

Collection of patient data. A case report form with 55 variables, including demographics, history, procedural characteristics, and outcomes of patients, was developed by a core group and agreed upon by the participating sites. Patients who underwent viv-TAVI were identified from the local TAVI database at the individual institution. Patient data were retrospectively collected by physician review of hospital charts and entered into a paper case report form that was faxed or e-mailed to the coordinating site at the University of Duisburg–Essen in Essen, Germany. Case report forms were reviewed for clinical face validity and analytical internal validity by the lead author (H.E.). All inconsistencies were resolved by contacting the local investigators. On-site monitoring for data validation was not performed. All data were manually entered into a Microsoft Excel database for further analysis.

Viv-TAVI procedure. Valve-in-valve TAVI was performed either transapically or transfemorally, as previously described (16–18). The balloon-expandable, trileaflet bovine stent valve (Edwards Sapien, and later, Edwards Sapien XT, Edwards Lifesciences, Irvine, California) was available for both transapical and transfemoral TAVI, whereas the self-expandable, trileaflet porcine pericardial tissue stent-valve (Medtronic CoreValve Revalving System, Minneapolis, Minnesota) was available only for retrograde transfemoral or trans-subclavian access.

Transapical viv-TAVI was performed using a left anterolateral minithoracotomy in the fifth or sixth intercostal space. After placement of left ventricular apical purse-string sutures and puncture of the left ventricle, a standard guidewire was advanced across the aortic arch down to the descending aorta using a Judkins right coronary catheter and exchanged for a stiff guidewire. Balloon valvuloplasty of the degenerated surgical bioprosthesis was left at the discretion of the operator and was performed only in case of stenotic physiology. Angiographic imaging was aligned in a perpendicular plane with the wire frame of the degenerated bioprosthesis. A crimped Edwards Sapien valve was advanced into the bioprosthesis and positioned under angiographic guidance. Finally, the valve was implanted under rapid right ventricular pacing to minimize movement (Fig. 1). After angiographic confirmation of stable and successful implant position, the sheath was retrieved and the left ventricular apex was closed as previously described (18).

Abbreviations and Acronyms

CAD = coronary artery disease

NYHA = New York Heart Association

STS = Society of Thoracic Surgeons

TAVI = transcatheter aortic valve implantation

TEE = transesophageal echocardiography

viv = valve-in-valve

For transfemoral viv-TAVI, either percutaneous or surgical access to the left or right common femoral artery was obtained. For percutaneous procedures, vascular closure devices (Prostar or Perclose Proglide, Abbott Vascular, Abbott Park, Illinois) were used in a pre-close technique (19). The degenerated bioprosthesis was crossed, usually using an Amplatz left coronary catheter, and a stiff guidewire was placed deep into the apex of the left ventricle. Balloon valvuloplasty of the degenerated surgical bioprosthesis before valve implantation was left at the discretion of the operator. After insertion of an 18- to 24-F sheath, the delivery system containing the crimped TAVI valve was

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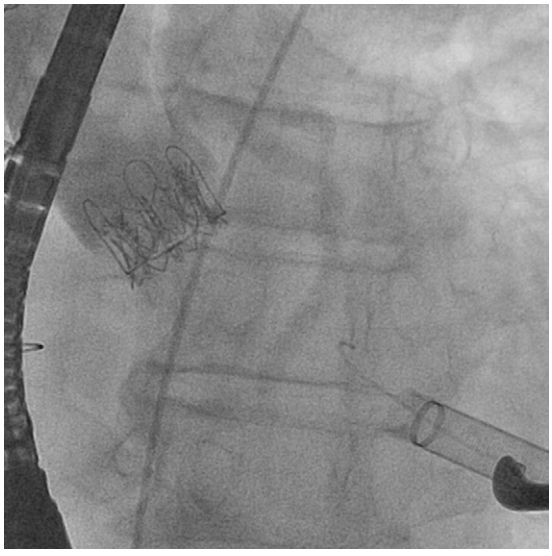

Figure 1. Post-Procedural Result of TA Viv-TAVI Using the Balloon-Expandable Edwards Sapien Valve

Viv-TAVI was performed for a failed Carpentier Edwards bioprosthesis. TA = transapical; TAVI = transcatheter aortic valve implantation; Viv = valve-in-valve.

advanced into the degenerated bioprosthesis. After positioning using fluoroscopic and angiographic and/or echocardiographic guidance, the balloon-expandable stent valve was deployed by balloon inflation under rapid right ventricular pacing at 160 to 220 beats/min (Fig. 2), whereas the self-expandable prosthesis was deployed stepwise and under guidance by several small-volume angiograms with and without accelerated pacing (110 to 130 beats/min) (Fig. 3). After confirmation of the correct position of the valve, the introducer sheath was withdrawn, and access closure was performed according to the local institutional protocol.

Figure 3. Post-Procedural Result of TF Viv-TAVI Using the Self-Expandable Medtronic CoreValve Revalving System

Viv-TAVI was performed for a failed Mitroflow bioprosthesis (Sorin Group, Milan, Italy). TF = transfemoral; other abbreviations as in Figure 1 (Online Video 1).

Statistical analysis. Categorical data are presented as frequencies; continuous variables are expressed as mean ± SD or median and range. Comparisons between groups were made with the chi-square or Fisher exact test (when cell count was <5) for categorical variables and the 2-sided Student *t* test for continuous variables. Multiple testing analysis was performed using ANOVA using the Bonferroni correction for post hoc analysis. Estimates of unadjusted overall survival were determined using the Kaplan-Meier nonparametric method. A p value of <0.05 was considered statistically significant. All

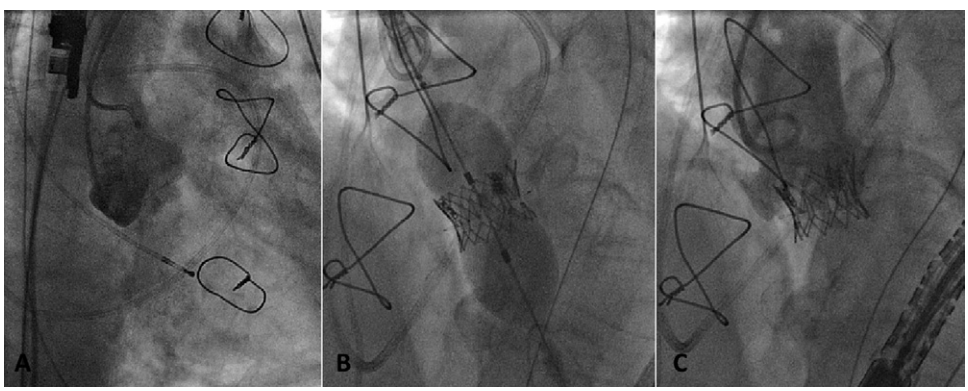

Figure 2. Transfemoral Viv-TAVI Using the Balloon-Expandable Edwards Sapien XT Valve

Viv-TAVI was performed in a patient with a failed Carpentier Edwards Perimount bioprosthesis (Edwards Lifesciences) and with severe valvular regurgitation **(A–C)**. Abbreviations as in Figure 1.

statistical analyses were performed using the SPSS software package (version 17.0, SPSS, Chicago, Illinois).

Results

Between 2005 and November 2010, a total of 1,545 TAVI procedures were performed at the participating centers. Among these, 47 (3%) patients underwent viv-TAVI for degenerated bioprostheses.

Patient demographics. Patient demographics are summarized in Table 1. Mean age of the patients was 80.3 ± 7.1 years, with most patients (60%) being males. The logistic euroSCORE ranged between 8.5% and 88.9%, with a mean of 35.0% ± 18.5%. Almost all patients were severely symptomatic, with 45 of 47 (96%) patients in New York Heart Association (NYHA) functional class ≥III before TAVI.

Degenerated bioprosthetic heart valves. Tissue valve failure affected 47 aortic surgical bioprostheses (Table 2); a single patient underwent simultaneous viv-TAVI for degenerated aortic and mitral bioprostheses. Indications for viv-TAVI included isolated xenograft stenosis in 22 (47%) patients, isolated severe regurgitation of the bioprosthesis in 15 (32%) patients, and mixed stenosis and regurgitation in the remaining 10 (21%) patients. At baseline, the mean gradient across the bioprosthesis was 38 ± 15 mm Hg, and the valve orifice area was 0.90 ± 0.42 cm^2. Bioprostheses had been implanted surgically 113 ± 65 (9 to 261) months before viv-TAVI.

Procedural data. Twenty-two (47%) patients underwent transapical viv-TAVI, whereas the remaining 25 (53%) were treated transfemorally (Table 3). The logistic euroSCOREs of patients undergoing transapical procedures were not significantly higher than in those patients treated transfemorally (38.8 ± 19.2% vs. 31.6 ± 17.5%, p = 0.185). The Edwards Sapien prosthesis was used in 75% of patients, with the remaining undergoing viv-TAVI with the Medtronic CoreValve valve (Figs. 1, 2, and 3). General anesthesia was used in 17 (36%) patients (all transfemoral TAVI).

In all patients, at least 1 stent valve was successfully implanted into the failed surgical bioprosthesis. Implantation height of TAVI prosthesis within the bioprosthesis was judged as "ideal" by the operator in 92% of patients, but 4 (8%) were judged as being implanted too low. After implantation, the mean transvalvular gradient was significantly reduced to 17 ± 10 mm Hg, whereas the aortic valve area was increased to 1.61 ± 0.47 cm^2 (p < 0.001 vs. baseline) (Table 3). However, 15 (44%) of 34 patients with available data on transvalvular gradients after viv-TAVI had increased mean transvalvular gradients ≥20 mm Hg (Table 4). Patients with increased transvalvular gradients ≥20 mm Hg after viv-TAVI had smaller surgical bioprosthetic diameters as compared with patients with lower final gradients (22.3 ± 1.2 mm vs. 23.7 ± 2.0 mm, p = 0.029). Conversely, it appeared that patients with small surgical bioprostheses had higher final transvalvular gradients after viv-TAVI (21 mm: 19.9 ± 10.2 mm Hg; 23 mm: 18.5 ± 8.4 mm Hg) than those with greater bioprostheses (≥25 mm: 8.9 ± 8.2 mm Hg, p = 0.035 vs. 21 mm; p = 0.048 vs. 23 mm). The relation of the TAVI prosthesis diameter to the diameter of the surgical bioprostheses ("prosthesis-to-prosthesis match" [20]) was, however, not different between patients with and without elevated transvalvular gradients (1.06 ± 0.07 vs. 1.02 ± 0.02, p = 0.254).

Table 1. Patient Demographics (N = 47)

Age, yrs	79.8 ± 7.1 (63–97)
Females	19 (40%)
CAD	28 (60%)
Previous myocardial infarction	12 (26%)
Previous CABG	16 (34%)
Previous PCI	8 (17%)
Diabetes mellitus	13 (28%)
Chronic renal failure	28 (60%)
Requiring dialysis	4 (9%)
Creatinine at baseline, mg/dl	1.7 ± 1.2 (0.6–6.9)
Logistic EuroSCORE, %	35.0 ± 18.5 (8.5–88.9)
STS score, %	11.6 ± 8.5 (2.2–34.9)
NYHA functional class before TAVI	
Class I	0
Class II	2 (4%)
Class III	39 (83%)
Class IV	6 (13%)
Left ventricular ejection fraction, %	52 ± 12 (17–70)

Values are mean ± SD (range) or n (%).
CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons; TAVI = transcatheter aortic valve implantation.

Table 2. Bioprosthetic Heart Valve Data (N = 47)

Position of the treated bioprosthesis	
Aortic	47 (100%)*
Type of surgical bioprosthesis	
Stented valve	45 (96%)
Stentless aortic root valve	2 (4%)
Diameter of surgical bioprosthesis,† mm	23
Time since valve replacement surgery, months	113 ± 65 (9–261)
Mean transbioprosthetic gradient before TAVI, mm Hg	38 ± 15 (9–73)
Valve orifice area (cm^2)	0.90 ± 0.42 (0.40–2.50)
Regurgitation across bioprosthesis before TAVI	
None	11 (23%)
Mild	11 (23%)
Moderate	7 (15%)
Severe	18 (38%)
Mode of failure of the bioprosthesis prompting TAVI	
Stenosis	22 (47%)
Regurgitation	15 (32%)
Mixed stenotic/regurgitation	10 (21%)

Values are n (%), median, or mean ± SD (range). *A single patient received simultaneous valve-in-valve transcatheter aortic valve implantation (TAVI) of aortic and mitral bioprostheses. †According to the manufacturer.

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Table 3. Procedural Data (N = 47)

Prosthesis used for viv-TAVI	
Edwards Sapien	35 (75%)
23 mm	29
26 mm	6
Medtronic CoreValve Revalving System	12 (25%)
26 mm	11
29 mm	1
Approach	
Transapical	22 (47%)
Transfemoral	25 (53%)
General anesthesia	17 (36%)
Use of intraprocedural TEE	31 (66%)
Valvuloplasty before TAVI	24 (51%)
Procedural success	46 (98%)
Implantation height*	
Ideal	43 (92%)
Too low	4 (9%)
Balloon dilation after TAVI	1 (2%)
Mean gradient after TAVI, mm Hg	17 ± 10 (3–35)
Valve orifice area after TAVI, cm^2	1.61 ± 0.48 (0.90–3.20)
Regurgitation after TAVI	
None	26 (55%)
Mild	20 (43%)
Moderate	1 (2%)
Severe	0

Values are n (%), n, or mean ± SD (range). *as judged by the operator.
TAVI = transcatheter aortic valve implantation; TEE = transesophageal echocardiography; viv = valve-in-valve.

With respect to valve competence, none or only mild regurgitation was observed in 46 of the 47 patients (98%) at the end of the procedure, with no case of moderate or severe regurgitation (Fig. 4). During the procedure, however, severe regurgitation occurred in 2 patients, requiring bail-out implantation of a second TAVI prosthesis during the same index procedure: In 1 male patient, severe central regurgitation was observed after transapical implantation of an Edwards Sapien valve, requiring implantation of another Edwards Sapien valve ("valve-in-valve-in-valve"). In the second patient, implantation of a 29-mm Medtronic CoreValve prosthesis resulted in too low a position with severe paravalvular regurgitation. Therefore, a second Medtronic CoreValve prosthesis was implanted with good result.

A single patient died during the procedure as a result of refractory low-output cardiac failure (Table 3). Procedural complications occurred in 9 (19%) patients and predominantly concerned vascular access complications in 6 of these 9 patients (Table 4).

Post-procedural outcome. After TAVI, patients were stabilized at the intensive care unit for a median of 2 days (Table 5). During the in-hospital period, 16 (34%) patients developed additional complications, such as renal failure requiring dialysis in 4 (9%) patients. New permanent pacemaker implantation was performed in 5 (11%) patients. The rate of new pacemaker implantation was nonsignificantly higher in patients undergoing Medtronic CoreValve implantation compared with those undergoing implantation of an Edwards Sapien valve (33% vs. 6%, p = 0.109). Other complications included low-output cardiac failure (n = 3), infectious complications (e.g., pneumonia, n = 3), or bleeding at the transapical access site requiring surgical revision (n = 1). The all-cause 30-day mortality rate was 17% (1 procedural and an additional 7 in-hospital deaths). Deaths were related to cardiac causes in 5 patients (low-output cardiac failure in 4, arrhythmia in 1). Death in the 3 remaining patients was related to sepsis arising during the post-operative phase.

Survivors versus nonsurvivors. Nonsurvivors were significantly older, had higher logistic euroSCOREs and STS scores, and had decreased left ventricular function than those surviving the in-hospital period (Table 6). Five of the 8 deaths occurred during the early experience (first half of the patients). Thirty-day mortality in patients undergoing transfemoral TAVI was nonsignificantly lower than in patients undergoing transapical TAVI (12% vs. 22.7%, p = 0.446). Interestingly, mortality rates were higher among patients with coronary artery disease (CAD) than among those without CAD (21.4% vs. 5.6%, p = 0.031), among patients with previous coronary intervention (37.5% vs. 10.8%, p = 0.085), and patients in chronic renal failure at baseline (75% vs. 0%, p = 0.018). The small number of patients and events, however, precluded any meaningful multivariate analysis.

Follow-up. Forty patients were finally discharged after a median in-hospital stay of 8 days. Patients surviving the in-hospital period showed significant symptom relief after TAVI, with only a single (2%) patient remaining in NYHA functional class >III compared with baseline when most patients (45 of 47 [96%]) were in NYHA functional class ≥III (p < 0.01) (Fig. 5). Figure 6 shows the Kaplan-Meier survival curve of patients undergoing viv-TAVI.

Discussion

The present registry comprises the largest experience with viv-TAVI for degenerated aortic bioprostheses reported so far. Our results were obtained in a "real-world" environment and confirm the feasibility of both the transfemoral and transapical approaches for the treatment of failed aortic bioprostheses observed in previous studies (11,12,14). Valve-in-valve TAVI resulted in a significant improvement of symptom status in almost all patients. Valvular function after viv-TAVI was excellent with respect to valve competence; however, elevated transvalvular gradients ≥20 mm Hg were observed in 44% of patients, particularly in those with degenerated surgical bioprostheses of small diameters. In the present series of high-risk patients for redo surgery, with a mean age of 80 years and a mean logistic euroSCORE of 35.0%, viv-TAVI was associated with incident risks of major complications and death. Overall

Table 4. Individual Surgical Bioprosthesis Data and Hemodynamic Results After Viv-TAVI

Surgical Bioprosthesis	Labeled Size	Mode of Bioprosthesis Failure	Implanted TAVI Prosthesis	Transvalvular Gradient at Baseline (mm Hg)	Transvalvular Gradient After Viv-TAVI (mm Hg)	Aortic Regurgitation at Baseline (Grade 0–3)	Aortic Regurgitation After Viv-TAVI (Grade 0–3)
CE Perimount	21 mm	Stenosis	ES 23 mm	47	21	0	0
		Stenosis	ES 23 mm	45	8	0	0
		Mixed	ES 23 mm	48	32	3	1
CE Perimount	23 mm	Stenosis	ES 26 mm	55	24	0	1
CE Perimount	25 mm	Insufficiency	ES 26 mm	28	7	3	1
		Insufficiency	ES 26 mm	16	30	3	0
		Mixed	ES 26 mm	44	8	3	1
CE Perimount Magna	25 mm	Insufficiency	ES 23 mm	25	6	3	0
CE Porcine	23 mm	Stenosis	ES 23 mm	27	12	1	0
CE Porcine	27 mm	Insufficiency	ES 23 mm	9	3	3	0
MDT Hancock II	21 mm	Insufficiency	CV 26 mm	15	10	3	2
MDT Hancock II	23 mm	Mixed	ES 23 mm	54	35	2	0
		Stenosis	ES 23 mm	26	12	0	0
		Stenosis	ES 23 mm	53	18	1	0
		Stenosis	ES 23 mm	31	7	1	0
		Insufficiency	ES 23 mm	27	20	3	1
		Stenosis	ES 23 mm	55	35	0	0
MDT Hancock II	25 mm	Insufficiency	ES 23 mm	11	5	2	0
MDT Mosaic	21 mm	Insufficiency	CV 26 mm	20	5	3	0
MDT Mosaic	23 mm	Insufficiency	ES 23 mm	29	25	3	0
MDT Mosaic Ultra	25 mm	Stenosis	ES 23 mm	32	11	0	0
SJM Biocor	23 mm	Stenosis	ES 23 mm	32	25	0	0
		Insufficiency	CV 26 mm	44	14	2	1
SJM Biocor	25 mm	Insufficiency	ES 23 mm	44	6	2	1
SJM Epic	23 mm	Stenosis	ES 23 mm	49	29	0	0
Sorin Mitroflow	21 mm	Mixed	ES 23 mm	56	30	3	1
		Mixed	ES 23 mm	53	18	3	1
		Stenosis	ES 23 mm	35	20	1	1
		Mixed	CV 26 mm	73	20	2	0
Sorin Mitroflow	23 mm	Stenosis	ES 23 mm	42	11	0	1
		Insufficiency	ES 23 mm	12	5	3	0
		Stenosis	ES 23 mm	45	20	1	0
		Stenosis	ES 23 mm	45	20	1	0

CE = Carpentier Edwards; CV = CoreValve; ES = Edwards Sapien; MDT = Medtronic; SJM = St. Jude Medical; other abbreviations as in Table 3.

30-day mortality was 17%, with 5 of the 8 patients dying within the first 30 days of being treated transapically. Three of the 8 fatalities were related to post-operative infectious or septic complications, perhaps a reflection of the severely reduced general health status of these frail elderly patients and associated inadequacies (resulting from a paucity of data) in post-TAVI care of these patients. These elderly comorbid patients were also prone to distinct complications that occurred in every third patient during the in-hospital period.

Bioprosthetic heart valves reduce the risks associated with lifelong oral anticoagulation and are therefore often favored over mechanical valves, particularly in elderly patients undergoing conventional valve replacement surgery (7,8). With time, however, this advantage is offset by degeneration of the bioprosthetic valve tissue, eventually resulting in failure of the tissue valve with either severe stenosis or valvular incompetence. Reoperation has been the standard treatment for failed tissue heart valves, but this exposes the patient to the risks associated with redo cardiac surgery. In patients with mean ages ranging from 56 to 64 years, the risk of death for redo surgery has been estimated to be 3.8% to 5.2% (21–23). However, bioprosthesis failure usually occurs several years after initial surgery, and the risk of redo surgery may thus be further increased as patients have become older and more comorbid in the meantime. Previous animal studies as well as selected patient series have supported the feasibility and/or safety of using viv-TAVI for failed bioprosthetic aortic valves (8,11,12,14). The series of Kempfert et al. (12) as well as the series from Webb et al. (11) have demonstrated that these elderly patients (mean

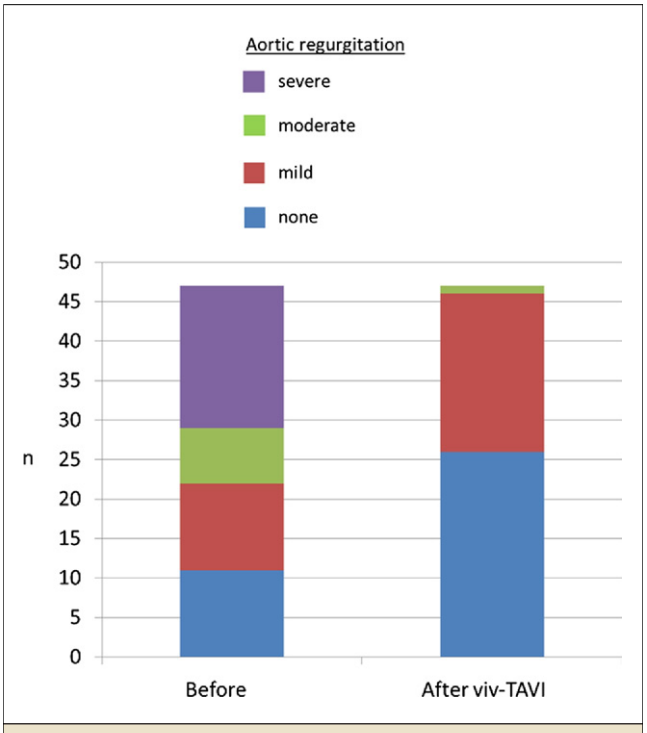

Figure 4. Valvular Competence Before and After Viv-TAVI

Abbreviations as in Figure 1.

Table 5. Procedural and In-Hospital Complications and Deaths (N = 47)

Procedural complications	9 (19%)
Vascular access complications	6 (13%)
Bail-out implantation of 2nd TAVI prosthesis	2 (4%)
Need for mechanical resuscitation	2 (4%)
Refractory cardiac output failure	1 (2%)
Stroke	0
Conversion to open surgery	0
Valve embolization	0
Procedural death	1 (2%)
Days on the intensive care unit	2 (1–28)
Days in-hospital	8 (3–28)
Additional in-hospital complications	16 (34%)
Renal failure requiring dialysis	4 (9%)
Arrhythmias	3 (6%)
New pacemaker implantation	5 (11%)
Cardiac complications	3 (6%)
Infections/septic complications	3 (6%)
Bleeding requiring re-thoracotomy	1 (2%)
In-hospital deaths (including proc. deaths)	8 (17%)
NYHA functional class at discharge	
I	12 (26%)
II	25 (53%)
III	1 (2%)
IV	0

Values are n (%) or median (range).
proc. = procedural; other abbreviations as in Table 1.

age 78 and 82 years, respectively) may even undergo viv-TAVI without mortality, although these series probably represented small numbers of highly selected cases from expert institutions.

Our data extend the findings of these previous reports, supporting the feasibility and high success rates for viv-TAVI for bioprosthetic valve failure in "real-world" clinical practice. In our multicenter experience, viv-TAVI was, however, associated with a 30-day mortality of 17% (8 of 47 patients), an observation that merits some further discussion. Given that patients were quite old (mean age: 80.3 years) with a high rate of comorbid conditions and predicted mean 30-day mortality based on a logistic euroSCORE of 35%, this mortality rate appears at the very least to be comparable (perhaps somewhat better) with that expected with redo valve replacement in this cohort. Nonetheless, mortality in the present series was somewhat higher than that observed in the series by Webb et al. (11) and Kempfert et al. (12). Although the lower mortality in these 2 small series may be a play of chance, it is also likely that inexperienced operators with lower volume and a different patient case mix than in the present registry originating from sites involved in pioneering the TAVI technique and with experienced, large-volume operators may have accounted for at least some of the differences in the mortality between our registry and the 2 case series mentioned in the previous text (11,12). Additionally, it should be noted that 5 of 8 patients who died the first 30 days underwent transapical viv-TAVI. Our results also suggest that improvements of post-operative patient care may have significant impact on outcomes after viv-TAVI. Three of the 8 fatalities were in fact related to septic complications (e.g., pneumonia) arising only in the post-operative course, highlighting the difficulties of managing these elderly and fragile patients after a technically successful viv-TAVI procedure.

Valve function after viv-TAVI intuitively represents an important marker of procedure success and will have a significant impact on subsequent patient outcomes (7). In the present registry, valvular function at the end of the viv-TAVI procedure was excellent with respect to valve competence. In

Table 6. Nonsurvivors Versus Survivors

	Nonsurvivors (n = 8)	Survivors (n = 39)	p Value
Age, yrs	82.2 ± 4.6	79.9 ± 7.5	0.422
Males	6 (75%)	21 (54%)	0.525
Log EuroSCORE, %	56.6 ± 22.4	30.5 ± 14.2	<0.001
Known CAD	6 (75%)	22 (56%)	0.031
Previous PCI	3 (38%)	5 (13%)	0.085
Previous CABG	2 (25%)	14 (36%)	0.697
Diabetes	3 (38%)	10 (26%)	0.673
Chronic renal failure	8 (100%)	20 (51%)	0.018
Left ventricular ejection fraction, %	45 ± 13	53 ± 12	0.083
Transapical viv-TAVI	5 (63%)	17 (44%)	0.446

Values are mean ± SD or n (%).
Log = logistic; other abbreviations as in Tables 1 and 3.

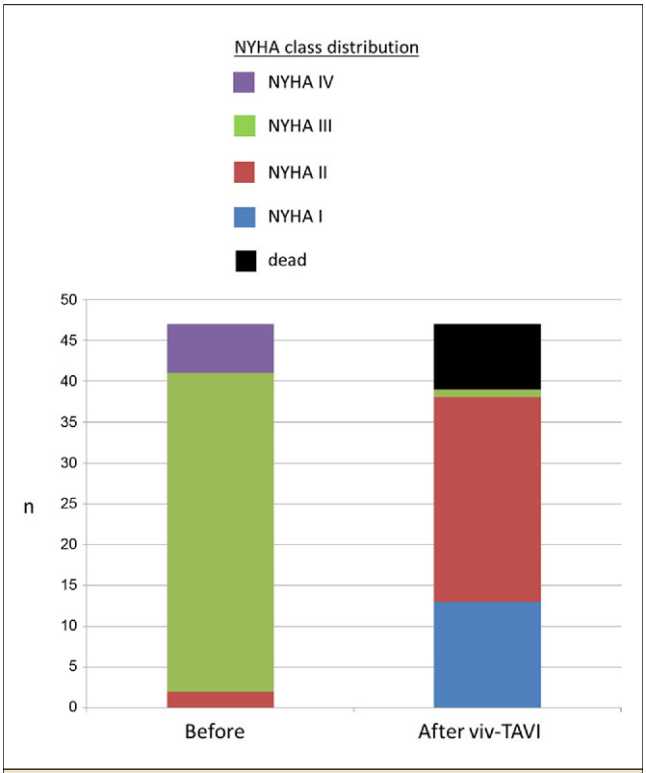

Figure 5. Improvement in Functional Status After Viv-TAVI

NYHA = New York Heart Association; other abbreviations as in Figure 1.

only a single patient was moderate regurgitation observed, without any case of severe aortic regurgitation. This is very similar to the previous reports from Webb et al. (11) and Kempfert et al. (12) who observed none or only mild regurgitation in all of their patients after viv-TAVI. It should, however, be noted that severe regurgitation was observed in 2 of the 47 (4%) patients during the procedure, necessitating bail-out implantation of a second TAVI device during the same procedure ("valve-in-valve-in-valve"). In 1 case, this was due to central leakage after implantation of a balloon-expandable Edwards Sapien valve, presumably reflecting malfunction of the valve leaflets (24). In the second case, severe paravalvular regurgitation was observed after too low implantation of a Medtronic CoreValve prosthesis, necessitating implantation of a second Medtronic CoreValve prosthesis.

The mean transvalvular gradients in the present series were somewhat higher than previously observed after TAVI for native aortic valve stenosis (25–27). This observation is, however, similar to that of previous viv-TAVI series (11). In our series, the mean transvalvular gradient was 17 ± 10 mm Hg, but 44% of patients, in fact, had a mean transvalvular gradient ≥20 mm Hg after viv-TAVI. As compared with native aortic valve TAVI, the higher post-procedural gradients are somewhat expected, given that the TAVI valve prosthesis is not completely expanded but rather constrained within the smaller surgical bioprosthesis and may thus have higher transvalvular gradients and lower effective orifice areas than when relatively fully expanded in a native aortic annulus (7). Our analysis highlights that the size of the originally implanted surgical bioprosthesis plays the most important role for prediction of post-procedural transvalvular gradients. Smaller surgical bioprostheses of ≤23 mm labeled size tend to show higher gradients after viv-TAVI than larger (≥25 mm) bioprostheses. Furthermore, the design of the surgical bioprostheses may affect transvalvular gradients after viv-TAVI. Most interestingly, post-interventional gradients for specific types of surgical bioprostheses were not predictable and varied between individual patients. A trend toward lower gradients for Medtronic CoreValve viv-TAVI procedures in small, 21-mm bioprostheses compared with Edwards Sapien valves was seen, but has to be confirmed in the future.

The finding of elevated transvalvular gradients after viv-TAVI may raise concerns with respect to long-term durability of the viv-TAVI valve and therefore mandates close echocardiographic follow-up to detect early signs of deterioration of valve function during further course. Nonetheless, these gradients should be viewed in lieu of the fact that most of these patients had prohibitively high risk for redo aortic surgery and are much lower than those observed among patients undergoing palliative aortic valve balloon valvuloplasty for stenotic aortic bioprostheses, a procedure that may not even be applicable for regurgitant bioprosthetic valves, which constitutes a majority of the patients with bioprosthetic valvular dysfunction.

There is ongoing debate with regard to the best-suited valve prosthesis for viv-TAVI out of the currently available devices. As in our series, the balloon-expandable Edwards Sapien valve

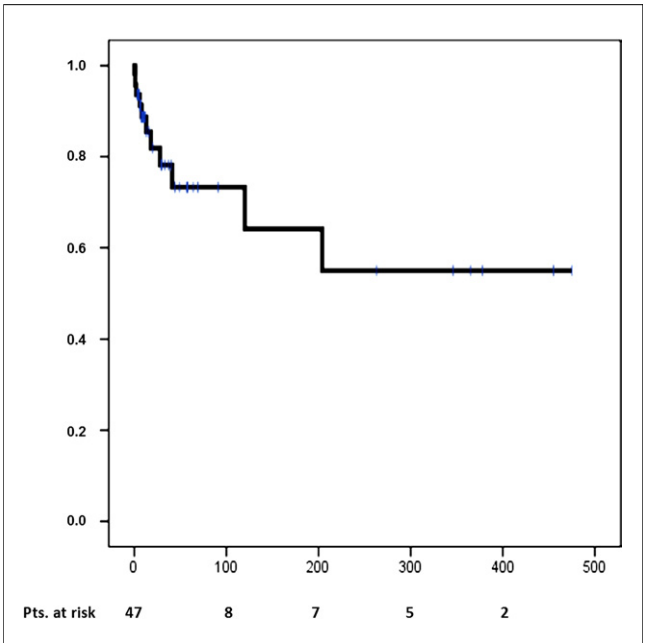

Figure 6. Kaplan-Meier Survival Curve of Patients Undergoing Viv-TAVI

Abbreviations as in Figure 1.

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has been used in most of the published viv series and case reports so far (11,12,14). It is speculated that this prosthesis may be better suited for this particular indication because of facilitated positioning and intra-annular implantation properties (12). Implantation of the Medtronic CoreValve prosthesis may be more demanding, and adjustment of prosthesis position during deployment may be hampered because of increased friction forces within the (metallic) ring of the surgical bioprosthesis. This may ultimately result in a noncorrectable too low position of the valve inside the surgical bioprosthesis, with subsequent severe paravalvular regurgitation, as occurred in a patient in our present series. Often, the surgical bioprosthesis offers a good landing zone for the Edwards Sapien valve (7). Alignment of the x-ray image with a perpendicular view allows for very precise positioning within the surgical bioprosthesis. In the presence of a degenerated stentless bioprosthetic heart valve (e.g., Elan valve, Vascutek, Inchinnan, United Kingdom), however, a rigid sewing ring for anchoring of the Edwards Sapien valve is missing, and a Medtronic CoreValve prosthesis may theoretically be preferable because of more secure anchoring of the prosthesis. Clearly, more information is needed to determine the best valve prosthesis for this indication.

Approximately 7% to 40% of patients undergoing TAVI for native aortic valve stenosis require implantation of a new pacemaker after the procedure for new-onset atrioventricular (AV) block (28,29). The rate of new pacemaker implantation of 11% in the present series was not prohibitive, but was higher than in previous series of patients undergoing viv-TAVI. In the series of Webb et al. (11) and Kempfert et al. (12), not even a single patient of the total of 21 patients undergoing viv-TAVI for degenerated aortic bioprosthesis required new implantation of a cardiac pacemaker after the procedure. The authors hypothesized that the rigid bioprosthetic sewing ring and valve frame protect the septal conduction tissues from injury at the time of TAVI (7,11). The present study may, however, suggest that the type of the valve device that it is used for viv-TAVI may influence the need for new pacemaker implantation after the procedure. The use of the self-expandable Medtronic CoreValve system was associated with a higher rate (33%) of new pacemaker implantation as compared with the implantation of the balloon-expandable Edwards Sapien valve (6%, $p = NS$), as was also observed previously after native-valve TAVI (29,30). The low rate of new pacemaker implantation observed by Webb et al. (11) and Kempfert et al. (12) may therefore simply reflect the exclusive use of the balloon-expandable Edwards valve in their series. Patients after viv-TAVI using the Medtronic CoreValve device, but also the Edwards valve, should thus be carefully monitored for a new atrioventricular block after the procedure, following the same recommendations as for native-valve TAVI.

Stroke is an inherent risk of TAVI for native calcified aortic valve stenosis. Previous studies have estimated the rate of clinically apparent stroke between 1% and 10%, whereas the incidence of clinically silent cerebral embolism during TAVI may even be much higher (16,31). In our series as well as in previous viv-TAVI series, the stroke rate was zero in a total now of 76 patients (12–14). Although we are unable to provide any mechanistic insight in to this favorably low rate of cerebrovascular complications based on our data, we can speculate some possible reasons for this in patients undergoing viv-TAVI. Degenerated surgical bioprostheses often are regurgitant and less calcified than native aortic valves, which are almost always stenotic and heavily calcified, particularly as most patients presenting for TAVI are significantly older. Thus, patients with bioprosthetic aortic valve dysfunction undergoing viv-TAVI require not only lower rates of pre-dilation with a balloon, but also less forceful dilation at lower atmospheric pressures and less aggressive manipulation than patients with native aortic valve dysfunction undergoing TAVI. As such, potentially a lower risk of periprocedural embolism may be anticipated. Future research using continuous intraprocedural transcranial Doppler may help to provide more insights into the differences in the embolic risk between TAVI for degenerated surgical bioprostheses and native aortic valve stenosis.

Clinical implications. Our multicenter registry confirms the findings of previous single-center experiences suggesting that transcatheter aortic valve implantation may be a promising alternative to redo surgery for degenerated surgically implanted tissue valves, particularly when the risk of surgery is high or prohibitive. The high, reproducible procedural success rate of viv-TAVI in the present registry, as well as in previous series, lends some additional credibility to this affirmation. Post-procedural complications and deaths appear to be high, but in fact, they are still acceptable when the predicted rates using the euroSCORE are considered. Additionally, the higher proportion of deaths related to sepsis may have further implications for improving outcomes of patients undergoing viv-TAVI. Development of appropriate and perhaps more aggressive strategies for post-operative patient management may help to reduce the incidence of periprocedural sepsis. Expected technical improvements of TAVI valves and delivery systems in the next 5 to 10 years and a growing understanding of optimal periprocedural management of these patients is likely to have a significant impact on outcomes of patients undergoing viv-TAVI. Finally, the possibility that not all currently available TAVI devices may be appropriate for viv-TAVI needs future evaluation.

Strengths and limitations. So far, the published literature on patients undergoing viv-TAVI is limited to reports of single cases or selected patient series. In contrast, our report represents by far the largest reported current experience with viv-TAVI for failed aortic bioprostheses. Our study should, however, be viewed in the light of its limitations. Most important, our analysis is a retrospective analysis of viv-TAVI cases. We were able to collect information on all patients during hospitalization and up to 30 days after the procedure. Data beyond this point were not available for all patients. Prospective, multicenter, large-scale registries (and perhaps randomized clinical trials comparing TAVI with surgery) are required to evaluate the short- and long-term safety and

efficacy of TAVI for this special indication in comparison with redo surgical valve replacement.

Conclusions

Our data indicate that viv-TAVI can be performed with high technical success rates and excellent post-procedural valvular function. However, in these elderly high-risk patients with multiple comorbidities, viv-TAVI was associated with 17% mortality that was related to septic complications in 3 of a total of 8 deaths. The already existing efforts at improving technology along with better post-operative management are likely to improve the future outcomes of viv-TAVI in this high-risk patient population.

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Key Words: aortic stenosis ■ bioprosthesis ■ surgery ■ TAVI ■ valve-in-valve.

APPENDIX

For an accompanying video, please see the online version of this article.