Outcomes of Redo Transcatheter Aortic Valve Replacement for the Treatment of Postprocedural and Late Occurrence of Paravalvular Regurgitation and Transcatheter Valve Failure

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Background—Transcatheter aortic valves can degenerate in a manner similar to surgical bioprostheses.

Methods and Results—Clinical and echocardiographic outcomes of patients who underwent redo transcatheter aortic valve replacement (TAVR) procedures >2 weeks post procedure were collected from 14 centers. Among 13 876 patients, 50 (0.4%) underwent redo TAVR procedure at participating centers. Indications for redo TAVR were moderate–severe prosthetic aortic valve stenosis (n=10, 21.7%), moderate–severe central prosthetic aortic valve regurgitation (n=13, 28.3%), and moderate–severe paraprosthetic aortic valve regurgitation (n=25, 50.0%). The index TAVR was most commonly a Medtronic CoreValve (N=38, 76.0%), followed by Edwards SAPIEN-type valves (n=12, 24.0%) and Portico (n=1, 2.0%). The redo TAVR device was most commonly a CoreValve/Evolut R (n=29, 58.0%), followed by a SAPIEN-type valve (n=20,40.0%) or a Boston Lotus valve (n=1, 2.0%). In 40 patients (80.0%), redo TAVR was performed using the identical device type or that of the succeeding generation. Valve performance was uniformly good after redo TAVR (mean transvalvular gradient post redo TAVR: 12.5±6.1 mm Hg). At hospital discharge, all patients remained alive, with 1 nondisabling stroke (2.0%) and 1 life-threatening bleed (2.0%). Permanent pacemaker implantation was required in 3 out of 35 patients without a prior pacemaker (8.6%). Late survival was 85.1% at a median follow-up of 1589 days (range: 31–3775) after index TAVR and 635 days (range: 8–2460) after redo TAVR.

Conclusions—Redo TAVR for the treatment of postprocedural and late occurrence of paravalvular regurgitation and transcatheter aortic valve prosthesis failure seems to be safe, and it is associated with favorable acute and midterm clinical and echocardiographic outcomes. **(*Circ Cardiovasc Interv*. 2016;9:e003930. DOI: 10.1161/CIRCINTERVENTIONS.116.003930.)**

Key Words: aortic regurgitation ■ aortic stenosis ■ degeneration ■ prosthesis ■ transcatheter aortic valve ■ transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) is an established alternative for patients with severe aortic stenosis.[1] There is a growing body of evidence demonstrating the durability of current TAVR devices out to 5 years.[2–5] However, it is well known that transcatheter aortic valves (TAVs) can degenerate in a manner similar to surgical bioprostheses.[6]

Received March 2, 2016; accepted August 3, 2016.

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Circ Cardiovasc Interv **is available at http://circinterventions.ahajournals.org** **DOI: 10.1161/CIRCINTERVENTIONS.116.003930**

WHAT IS KNOWN

- The surgical experience has taught us that the main concern with bioprostheses is their limited durability.
- As with surgical bioprostheses, transcatheter aortic valves can be expected to degenerate with time and may eventually require repeat intervention.
- It has been argued that implantation of a second transcatheter valve to treat nonacute transcatheter valve failure because of structural valve degeneration and significant paravalvular regurgitation can be an effective approach.

WHAT THE STUDY ADDS

- Failure of transcatheter prostheses may present as intraprosthetic regurgitation, stenosis, or paravalvular leak.
- In contrast with redo valve surgery, which is technically challenging and carries a higher mortality and morbidity risk than the primary valve procedure, redo transcatheter aortic valve replacement seems to be safe.

Implantation of a second TAV inside a previously implanted TAV (TAV-in-TAV technique) can be an effective technique to promptly treat acute implant failure.[7,8] In light of the favorable hemodynamic and clinical outcomes associated with the TAV-in-TAV procedure in this setting, it has been argued that this strategy can also be applied in the setting of nonacute TAVR failure because of structural valve degeneration and significant paravalvular regurgitation (PVR). To date, only a few anecdotal reports have demonstrated the feasibility of this approach.[9–12] The aim of this multicenter international collaboration was to examine the safety and the midterm efficacy of redo TAVR to treat postprocedural and late transcatheter valve failure.

Methods

Data collection was initiated in December 2014, with data from cases of redo TAVR performed before study initiation collected retrospectively and subsequent cases added prospectively. Patients met the inclusion criteria for the study if they were treated with a second TAVR at least 2 weeks after the index procedure. Data were collected from 14 centers across Italy, Germany, Canada, Spain, France, the Netherlands, and the United States using a dedicated case report form. Inconsistencies were resolved directly with local investigators and on-site data monitoring.

All patients gave written informed consent to the TAVR procedure and anonymous data collection and analysis. The authors are solely responsible for the design and conduct of this study, all analyses, drafting, editing of the article, and its final contents.

Statistical Analysis and Definitions

Descriptive statistics are reported as mean±SD for normally distributed continuous variables or as median and 25th–75th percentile (interquartile range) otherwise. Normality of distribution was tested by means of the Kolmogorov–Smirnov test. Absolute and relative frequencies are reported for categorical variables. Continuous variables were analyzed with the Student's *t* test or Wilcoxon rank-sum test depending on the variable distribution. The χ^2 test and the Fisher exact test were performed for categorical variables. Survival analysis has been performed with the Kaplan–Meier method, reporting incidence of event at each year. A repeated measures analysis with linear contrast at each time point was performed to assess mean aortic gradient change over time. All data were processed using the Statistical Package for Social Sciences, V.20 (SPSS, Chicago, IL). All outcomes were defined according to Valve Academic Research Consortium-2 criteria.[13] Reasons for redo TAVR were categorized into the following: (1) degeneration (defined as severe leaflet calcification or tissue ingrowth causing restrictive leaflet function or leaflet tear) and (2) PVR. Mechanism of TAV degeneration (ie, moderate–severe prosthetic aortic valve stenosis, moderate or severe intraprosthetic aortic valve regurgitation, or combined) was evaluated according to the Valve Academic Research Consortium-2 criteria. Patients with at least moderate degree of both stenosis and regurgitation were included in the combined group. Other patients were categorized according to the primary mechanism of degeneration, either in the stenosis group or in the regurgitation group.

Results

Patient Population

A total of 13 876 patients underwent TAVR at participating centers. Among these, 50 patients (0.4%) underwent redo TAVR. The clinical characteristics of this population are showed in Table 1. Figure 1 depicts the modes of failure that led to redo TAVR. The indication for redo TAVR was moderate–severe PVR in 25 patients and valve degeneration (new valve stenosis n=9, intravalvular regurgitation n=13, or combined n=3) in the remaining 25 patients. Endocarditis as the cause of intravalvular regurgitation was documented in one patient and suspected in another one (patient was found with leaflet tear, and blood cultures were not performed). Median age was 78 years (interquartile range 71–89), and 16 (32.0%) were females. Mean Society of Thoracic Surgery score was 9.2±8.9%. The mean interval between the index TAVR and redo TAVR was 812±750 days (Figure 2). This interval was significantly lower in patients undergoing redo TAVR for PVR, as compared with patients experiencing structural valve failure (ie, valve stenosis or intravalvular regurgitation; 435±594 versus 1189±706 days; $P<0.001$). New York Heart Association functional class III or IV dyspnea was the most frequent clinical presentation (n=36, 72.0%), followed by acute heart failure (n=7, 14.0%). In 7 patients (14.0%), symptoms were mild (New York Heart Association class II), and late TAV degeneration was recognized at scheduled echocardiographic follow-up.

Procedure

Procedural data for both index and redo TAVR procedures are reported in Tables 2 and 3. For the index TAVR, the most common device was CoreValve (Medtronic Inc, Galway, Ireland; N=37, 74.0%), followed by Edwards SAPIEN (N=8, 16.0%), SAPIEN XT (N=2, 4.0%), SAPIEN 3 (N=2, 4.0%; Edwards Lifesciences, Irvine, CA), and Portico (St Jude Medical, Minneapolis, MN; N=1, 2.0%). For redo TAVR, devices used were CoreValve (N=28, 56.0%), SAPIEN XT (N=14, 28.0%), SAPIEN 3 (N=6, 12.0%), Evolut R (Medtronic Inc; N=1, 2.0%), and Lotus valve (Boston Scientific Corporation, Natick, MA; N=1, 2.0%).

In 40 patients (80.0%), redo TAVR was performed using the identical device type or that of the succeeding generation

Table 1. Baseline Characteristics

	All (n=50)	Degeneration* (n=25)	PVR (n=25)	*P* Value
Age, y	76.3±8.9	74.7±10.3	77.9±7.2	0.204
Female, n (%)	16 (32.0)	9 (36.0)	7 (28.0)	0.544
Diabetes mellitus, n (%)	12 (24.0)	5 (20.0)	7 (28.0)	0.508
COPD, n (%)	12 (24.0)	8 (32.0)	4 (16.0)	0.185
Prior stroke, n (%)	4 (8.0)	3 (12.0)	1 (4.0)	0.305
PVD, n (%)	15 (30.0)	7 (28.0)	8 (32.0)	0.758
Prior CABG, n (%)	14 (28.0)	4 (16.0)	10 (40.0)	0.059
Permanent AF, n (%)	12 (24.0)	5 (20.0)	7 (28.0)	0.508
Chronic renal failure, n (%)	12 (24.0)	6 (24.0)	6 (24.0)	1.000
Dialysis, n (%)	2 (4.0)	2 (8.0)	0 (0.0)	0.245
Liver cirrhosis, n (%)	3 (6.0)	2 (8.0)	1 (4.0)	0.492
NYHA III/IV, n (%)	39 (78.0)	21 (84.0)	18 (72.0)	0.443
Malignancy, n (%)	4 (8.0)	2 (8.0)	2 (8.0)	1.000
Prior pacemaker, n (%)	9 (18.0)	4 (16.0)	5 (20.0)	0.500
STS score, %	9.2±8.9	7.2±7.2	11.1±10.1	0.175
LVEF, %	51.0±14.7	52.1±14.3	49.8±13.5	0.732
Mean aortic gradient, mm Hg	43.1±14.6	45.4±16.4	40.6±12.3	0.284

AF indicates atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; NYHA, New York Heart Association; PVD, peripheral vascular disease; PVR, paravalvular regurgitation; and STS, Society of Thoracic Surgery.

*Degeneration was defined as severe leaflet calcification or tissue ingrowth causing restrictive leaflet function or leaflet tear.

(Figure 3). In 43 patients (86.0%), the access routes for the redo procedure were the same as for the first TAVR. When both the index and the redo TAVR were transfemoral (n=40), the redo delivery sheath was most often inserted in the contralateral artery (n=33, 82.5%). Contrast media used for redo TAVR was considerably lower than that used during the first TAVR (188±89 versus 80±46 mL; $P<0.001$). Balloon postdilation was performed in 17 redo TAVR procedures (34.0%). One case (2.0%) of coronary occlusion after 26-mm SAPIEN XT implantation into a 26-mm Edwards-SAPIEN was reported. There was one (2.0%) 31-mm CoreValve embolization that occurred in an attempt to treat a failed 31-mm CoreValve. No aortic rupture was documented.

Clinical Outcomes

In-hospital complications of both index and redo TAVR procedures are reported in Table 4. After redo TAVR, all patients left the hospital alive. During hospitalization, one patient (2.0%) had a nondisabling stroke and another patient (2.0%) had a life-threatening bleeding, whereas new permanent

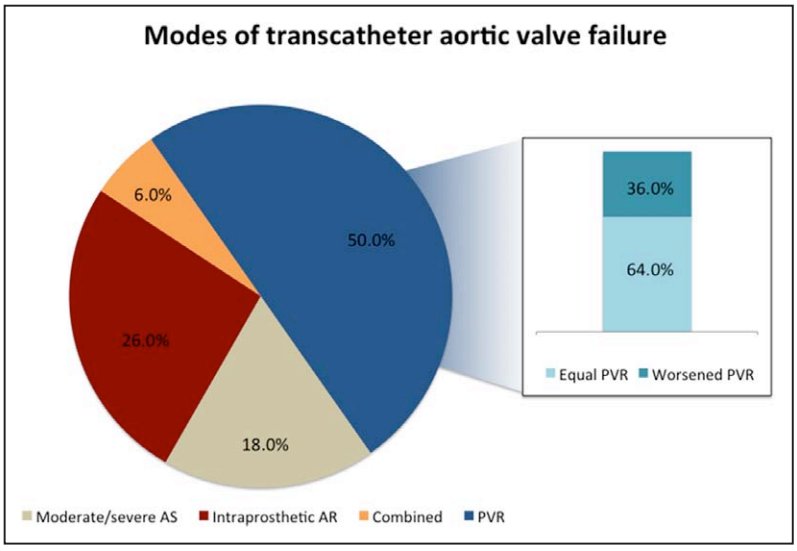

Figure 1. Modes of transcatheter aortic valve failure. PVR as main reason for redo TAVR is divided into 2 groups: patients with worsened PVR and patients with PVR that remained stable after the first TAVR until the redo procedure. AR indicates aortic regurgitation; AS, aortic stenosis; PVR, paravalvular regurgitation; and TAVR, transcatheter aortic valve replacement.

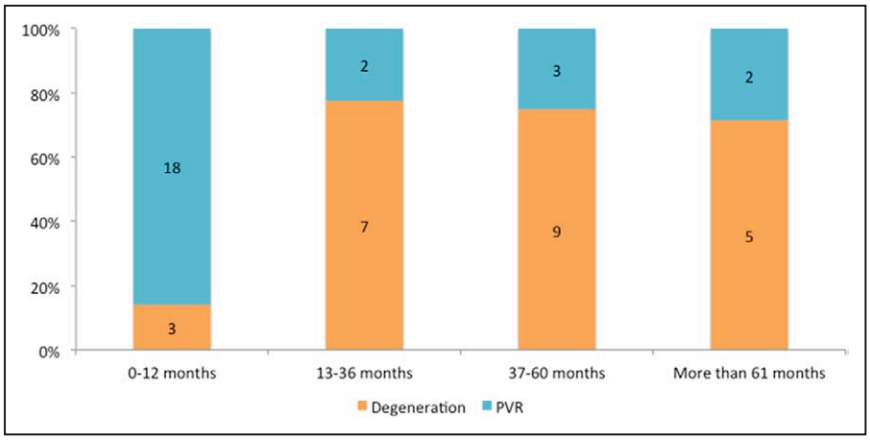

Figure 2. Timing of redo TAVR after the index procedure. The light blue bars and the yellow bars indicate patients who had paravalvular regurgitation (PVR) and degeneration, respectively, as the main reason of transcatheter aortic valve failure.

pacemaker implantation was required in 3 out of 35 (8.6%) patients without a pacemaker before redo TAVR. At a median follow-up of 1589 (range: 31–3775) and 586 (range: 8–2460) days after index and redo TAVR, respectively, survival was 85.1% (Figure 4).

Prosthesis Performance

Figure 5 and Table 5 demonstrate TAV performance at follow-up. Acutely after the first TAVR procedure, mean pressure gradients decreased from 43.7±15.5 mm Hg to 11.9±7.7 mm Hg. At the time of the diagnosis of valve failure, transvalvular gradients were increased in patients with valve degeneration (32.9±21.3 mm Hg), whereas they were consistent with the baseline values in patients presenting with significant PVR (12.3±5.0 mm Hg). After redo TAVR, gradients reduced markedly in patients with valve degeneration (15.1±6.7 mm Hg), even though they were slightly higher as compared with patients who had a second TAV implanted because of PVR (9.0±4.1 mm Hg). Moderately elevated intraprosthetic gradients (mean gradients ≥20 mm Hg) were reported in 5 patients with valve degeneration; in 1 of these, patient–prosthesis mismatch (mean gradient 40 mm Hg, aortic valve area 0.6 cm^2) was reported immediately

Table 2. Procedural Variables

Variables	Index TAVR (n=50)	Redo TAVR		
		All (n=50)	Degeneration* (n=25)	PVR (n=25)
Prosthesis type				
CoreValve, n (%)	37 (74.0)	29 (58.0)	13 (52.0)	16 (64.0)
Evolut R, n (%)	0 (0.0)	1 (2.0)	0 (0.0)	1 (4.0)
Edwards SAPIEN, n (%)	8 (16.0)	0 (0.0)	0 (0.0)	0 (0.0)
SAPIEN XT, n (%)	2 (4.0)	14 (28.0)	9 (36.0)	5 (20.0)
SAPIEN 3, n (%)	2 (4.0)	6 (12.0)	3 (12.0)	3 (12.0)
Portico, n (%)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lotus, n (%)	0 (0.0)	1 (2.0)	0 (0.0)	1 (4.0)
Access				
Transfemoral, n (%)	44 (88.0)	43 (86.0)	20 (80.0)	23 (92.0)
Trans-subclavian, n (%)	1 (2.0)	2 (4.0)	1 (4.0)	1 (4.0)
Transapical, n (%)	5 (10.0)	5 (10.0)	4 (16.0)	1 (4.0)
Predilation, n (%)	36 (72.0)	12 (24.0)	7 (28.0)	5 (20.0)
Postdilation, n (%)	15 (30.0)	17 (37.0)	4 (17.4)	13 (56.5)
Valve embolization, n (%)	0 (0.0)	1 (2.0)	0 (0.0)	1 (4.0)
Coronary occlusion, n (%)	0 (0.0)	1 (2.0)	1 (4.0)	0 (0.0)
Major vascular complications, n (%)	7 (14.0)	3 (6.0)	3 (12.0)	0 (0.0)
Minor vascular complications, n (%)	2 (4.0)	2 (4.0)	1 (4.0)	1 (4.0)
Closure failure, n (%)	2 (4.0)	1 (2.0)	1 (4.0)	0 (0.0)
Contrast dye, mL	188.8±89.4	80.6±46.3	78.1±53.1	82.9±40.2

PVR indicates paravalvular regurgitation; and TAVR, transcatheter aortic valve replacement.
*Degeneration was defined as severe leaflet calcification or tissue ingrowth causing restrictive leaflet function or leaflet tear.

Table 3. Procedural Variables and Reasons for Redo TAVR

Patients	Age		Index TAVR Device	Index TAVR Access	Redo TAVR Device	Redo TAVR Access	Reason for Redo TAVR	Etiology of Failure*	Timing Redo, days	Residual PVR	Residual AV Grad, mm Hg
	Index TAVR	Redo TAVR									
Patient 1	82	86	CV 26-mm	TF	SXT 23-mm	TF	Intraprosthetic AR	Degeneration	1351	None	15
Patient 2	72	75	CV 29-mm	TF	CV 29-mm	TF	Intraprosthetic AR	Degeneration	1245	Trivial	3
Patient 3	85	91	CV 26-mm	TF	CV 26-mm	TF	Moderate/severe AS	Degeneration	2051	Trivial	11
Patient 4	73	76	CV 31-mm	TF	CV 31-mm	TF	Intraprosthetic AR	Degeneration	1209	Mild	15
Patient 5	77	81	CV 29-mm	TF	CV 29-mm	TF	PVR	Worsened	1367	Moderate	12
Patient 6	53	54	CV 29-mm	TF	CV 29-mm	TF	Intraprosthetic AR†	Endocarditis	483	Moderate	14
Patient 7	64	64	CV 31-mm	TF	CV 31-mm	TF	PVR	Unchanged	161	Mild	15
Patient 8	65	66	CV 31-mm	TF	S3 29-mm	TF	Intraprosthetic AR	Degeneration	303	Trivial	21
Patient 9	88	88	S3 26-mm	TF	Lotus 27-mm	TF	PVR	Unchanged	58	Mild	9
Patient 10	82	82	CV 26-mm	TS	CV 26-mm	TF	PVR	Unchanged	204	Mild	13
Patient 11	78	79	CV 29-mm	TF	CV 29-mm	TF	PVR	Unchanged	120	Trivial	7
Patient 12	77	81	CV 26-mm	TF	CV 26-mm	TS	Intraprosthetic AR	Degeneration	1312	None	8
Patient 13	84	84	CV 29-mm	TF	CV 29-mm	TF	Intraprosthetic AR	Unknown	29	Trivial	NA
Patient 14	75	75	CV 29-mm	TF	CV 29-mm	TS	PVR	Unchanged	15	Mild	8
Patient 15	68	68	CV 29-mm	TF	CV 29-mm	TF	PVR	Unchanged	29	Trivial	7
Patient 16	86	86	CV 31-mm	TF	CV 29-mm	TF	PVR	Worsened	33	Mild	7
Patient 17	87	87	CV 31-mm	TF	CV 29-mm	TF	PVR	Worsened	17	Mild	9
Patient 18	78	79	CV 31-mm	TF	CV 29-mm	TF	PVR	Worsened	371	Trivial	19
Patient 19	78	78	CV 26-mm	TF	CV 23-mm	TF	Intraprosthetic AR	Unchanged	85	None	10
Patient 20	74	75	CV 29-mm	TF	CV 26-mm	TF	Intraprosthetic AR	Endocarditis	490	Trivial	5
Patient 21	82	82	CV 31-mm	TF	CV 29-mm	TF	PVR	Unchanged	15	Mild	8
Patient 22	84	86	CV 29-mm	TF	CV 29-mm	TF	PVR	Unchanged	399	Mild	9
Patient 23	77	82	CV 29-mm	TF	SXT 29-mm	TF	PVR	Unchanged	1824	Trivial	9
Patient 24	78	78	CV 26-mm	TF	SXT 26-mm	TF	PVR	Unchanged	54	Trivial	7
Patient 25	75	79	CV 29-mm	TF	SXT 26-mm	TF	Intraprosthetic AR	Degeneration	1263	Trivial	13
Patient 26	70	71	CV 29-mm	TF	SXT 26-mm	TF	PVR	Unchanged	371	Mild	15
Patient 27	65	70	CV 29-mm	TF	CV 29-mm	TF	Moderate/severe AS	Degeneration	1828	None	25
Patient 28	81	86	CV 29-mm	TF	CV 29-mm	TF	Moderate/severe AS	Degeneration	1731	None	21
Patient 29	82	84	CV 26-mm	TF	CV 26-mm	TF	Intraprosthetic AR	Unchanged	715	None	12
Patient 30	64	65	CV 31-mm	TF	CV 31-mm	TF	PVR	Worsened	272	Mild	10
Patient 31	76	78	ES 26-mm	TF	SXT 26-mm	TA	Moderate/severe AS	Degeneration	731	Mild	12
Patient 32	64	64	CV 31-mm	TF	SXT 29-mm	TA	PVR	Unchanged	161	None	10
Patient 33	72	77	SXT 26-mm	TA	SXT 26-mm	TA	Moderate/severe AS	Degeneration	1372	Trivial	19
Patient 34	76	77	ES 26-mm	TF	SXT 26-mm	TF	Moderate/severe AS	Unknown	427	None	23
Patient 35	52	55	ES 23-mm	TF	SXT 23-mm	TF	Combined AS/AR	Degeneration	889	None	30
Patient 36	63	67	ES 23-mm	TF	SXT 23-mm	TF	Moderate/severe AS	Degeneration	1387	None	15
Patient 37	76	80	CV 29-mm	TF	CV 29-mm	TF	PVR	Worsened	99	Trivial	17
Patient 38	84	88	ES 23-mm	TA	SXT 23-mm	TF	PVR	Unchanged	1244	None	11
Patient 39	78	78	CV 31-mm	TF	S3 29-mm	TF	PVR	Unchanged	33	Trivial	8
Patient 40	74	79	CV 29-mm	TF	CV 31-mm	TF	PVR	Worsened	1990	None	4
Patient 41	77	80	CV 29-mm	TF	CV 29-mm	TF	PVR	Worsened	1232	Trivial	4

(*Continued*)

Table 3. Continued

Patients	Age		Index TAVR Device	Index TAVR Access	Redo TAVR Device	Redo TAVR Access	Reason for Redo TAVR	Etiology of Failure*	Timing Redo, days	Residual PVR	Residual AV Grad, mm Hg
	Index TAVR	Redo TAVR									
Patient 42	75	83	CV 26-mm	TF	CV 26-mm	TF	Moderate/severe AS	Degeneration	2985	Trivial	10
Patient 43	72	74	CV 31-mm	TF	CV 31-mm	TF	PVR	Worsened	568	Mild	7
Patient 44	56	62	ES 23-mm	TF	SXT 23-mm	TF	Combined AS/AR	Degeneration	2031	None	9
Patient 45	73	75	ES 23-mm	TA	SXT 23-mm	TA‡	Intraprosthetic AR	Unknown	778	None	18
Patient 46	47	52	ES 26-mm	TF	S3 26-mm	TF	Moderate/severe AS	Degeneration	1372	None	14
Patient 47	70	71	Por 25-mm	TF	S3 26-mm	TF	PVR	Unchanged	69	Mild	8
Patient 48	81	81	S3 26-mm	TA	S3 29-mm	TF	PVR	Unchanged	195	Mild	9
Patient 49	72	77	SXT 23-mm	TA	S3 23-mm	TA	Combined AS/AR	Degeneration	1789	None	13
Patient 50	74	79	CV 26-mm	TF	Evolut 26-mm	TF	Intraprosthetic AR	Degeneration	1887	None	9

AR indicates aortic regurgitation; AS, aortic stenosis; AV Grad, aortic valve gradient; CV, CoreValve; ES, Edwards-SAPIEN; Por, Portico; PVR, paravalvular regurgitation; S3, SAPIEN 3; SXT, SAPIEN XT; TA, transapical; TAVR, transcatheter aortic valve replacement; TF, transfemoral; and TS, trans-subclavian.

*Degeneration was defined as severe leaflet calcification or tissue ingrowth causing restrictive leaflet function or leaflet tear.

†Patient had moderate PVR after the index procedure, which remained unchanged until the redo TAVR. The reason for redo TAVR was new intraprosthetic AR because of endocarditis.

‡Procedure performed through left anterior thoracotomy.

after the first TAVR. Of note, valve hemodynamics remained stable at follow-up (13.2±7.2 mm Hg and 8.8±4.3 mm Hg, respectively). Moderate/severe PVR after the index TAVR was a frequent finding in this particular population, being reported in 40.0% of cases. In 14 patients (70.0%) with moderate/severe PVR, severe or massive annular calcifications were reported. Low TAV implantation was the main mechanism of PVR in 11 cases (55.0%). In the remaining 9 cases (45.0%), the TAV was deployed at the proper height. Redo TAVR was successful at reducing PVR to mild or less in 23 out of 25 patients (92.0%), who presented with significant PVR before the second TAVR procedure. In the 2 cases of residual ≥moderate PVR after CoreValve-in-CoreValve, there was severe annular calcification. No cases of valve thrombosis were documented.

Discussion

Previous surgical series have demonstrated that most biological valves degenerate within 10 to 20 years.[14] Hypothetically, TAV leaflet trauma can occur because of transcatheter valve preparation and compression, balloon dilation, suboptimal leaflet coaptation, leaflet folding, or leaflet-frame contact because of asymmetrical frame expansion. Durability of transcatheter valves may thus be shorter than surgical bioprostheses.[6,15] The longest available clinical follow-up in a substantial number of

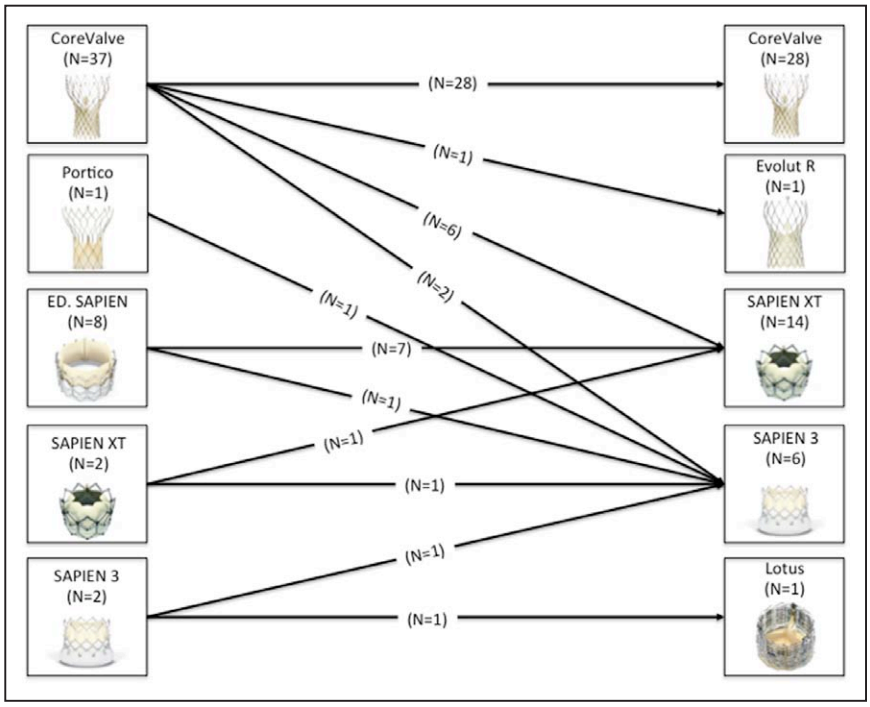

Figure 3. Transcatheter aortic valves implanted during the index TAVR (**left**) and the redo TAVR (**right**). TAVR indicates transcatheter aortic valve replacement.

TAVR patients is limited to 5 years, at which time, excellent valve performance has been demonstrated.[2–5] However, as with surgical bioprostheses, TAVs can be expected to degenerate with time and may eventually require repeat intervention.[16]

This multicenter study is the first showing that redo TAVR to treat postprocedural and late transcatheter valve failure is safe and associated with favorable clinical outcomes. Despite the presence of 2 transcatheter prostheses, valve performance was reassuring.

Failure of transcatheter prostheses may present as stenosis (as a consequence of calcification, pannus, or thrombosis) or as intraprosthetic regurgitation (as a consequence of reduced leaflet mobility, tears, or endocarditis). Failure may also present as PVR.[6] Although this is more frequently an acute complication, the importance of regurgitation may only become clinically evident after a period of time. In this population, the mode of failure that led to repeat TAVR procedure was well balanced among valve degeneration (including stenosis and intraprosthetic regurgitation) and PVR.

Selection of the redo TAV varied significantly across centers, suggesting that this procedure requires further study. However, important observations should be made: when a balloon-expandable TAV fails, implantation of a second same-sized balloon-expandable TAV was the most commonly used approach. Alternatively, implantation of a mechanical-expandable device may represent a reasonable strategy, performed in only one case. In fact, all cases of failed balloon-expandable valves were treated with the same device type and size, with the exception of one failed 26-mm SAPIEN 3 device treated with a 27-mm Lotus valve.[10] Because of the lack of cases reported in the study, it remains unknown the most appropriate strategy to treat PVR of a well-deployed balloon-expandable TAV. In contrast, this study showed that failed self-expanding TAV (CoreValve and Portico) treatment was more variable, with the same valve implanted in 76%, but a balloon-expandable valve in 28%. In terms of sizing, either the same or the smaller valve size was implanted. In the case of self-expanding TAV degeneration (ie, CoreValve or Portico), a second same-sized or smaller TAV (self-expanding, balloon-expandable, or mechanical-expandable) can be effectively implanted; a smaller TAV must be deployed at the level of the narrowest portion of the first prosthesis to obtain adequate anchoring and sealing. When the mechanism of CoreValve failure is PVR, there are 2 possible scenarios: (1) the PVR is mainly caused by too high or too low valve implantation; in this case, the deployment of any TAV type in the proper position is generally effective in reducing the leak; (2) the PVR is secondary to incomplete frame expansion or suboptimal sealing because of severe annular calcification; in this case, a second TAV with higher radial force (ie, SAPIEN or Lotus) would be preferred to obtain greater expansion and sealing. These considerations need to be proven in future studies.

In general, redo TAVR procedures were safe, with low rates of periprocedural complications and midterm survival comparable to recent TAVR series. We reported one case of coronary obstruction by the native calcified cusp, which occurred after SAPIEN XT implantation inside a degenerated Edwards SAPIEN valve (resolved by urgent stent implantation into the left main) and one case of 31-mm CoreValve embolization in an attempt to treat a failed 31-mm CoreValve.

Table 4. In-Hospital Outcomes

Variables	Index TAVR (n=50)	Redo TAVR		
		All (n=50)	Degeneration* (n=25)	PVR (n=25)
Death, n (%)	…	0 (0.0)	0 (0.0)	0 (0.0)
CV death, n (%)	…	0 (0.0)	0 (0.0)	0 (0.0)
Disabling stroke, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nondisabling stroke, n (%)	0 (0.0)	1 (2.0)	0 (0.0)	1 (4.0)
TIA, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
LT bleeding, n (%)	0 (0.0)	1 (2.0)	0 (0.0)	1 (4.0)
Major bleeding, n (%)	1 (2.3)	1 (2.0)	1 (4.0)	0 (0.0)
Minor bleeding, n (%)	5 (11.4)	8 (16.0)	3 (12.0)	5 (20.0)
Myocardial infarction, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
AKI stage 1, n (%)	2 (4.2)	2 (4.3)	2 (8.7)	0 (0.0)
AKI stage 2, n (%)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
AKI stage 3, n (%)	2 (4.2)	3 (6.5)	1 (4.3)	2 (9.5)
PM implantation, n (%)	6 (14.6)†	3 (8.6)‡	1 (5.9)	2 (11.1)
≥moderate PVR, n (%)	20 (40.0)	2 (4.0)	1 (4.0)	1 (4.0)

AKI after index TAVI was available in 48 patients. Bleeding after index TAVI was available in 44 patients. AKI indicates acute kidney injury; CV, cardiovascular; LT, life-threatening; PM, pacemaker; PVR, paravalvular regurgitation; TAVI, transcatheter aortic valve implantation; TAVR, transcatheter aortic valve replacement; and TIA, transient ischemic attack.

*Degeneration was defined as severe leaflet calcification or tissue ingrowth causing restrictive leaflet function or leaflet tear.

†Percentage calculated on 41 patients with no PM before the procedure.

‡Percentage calculated on 35 patients with no PM before the procedure.

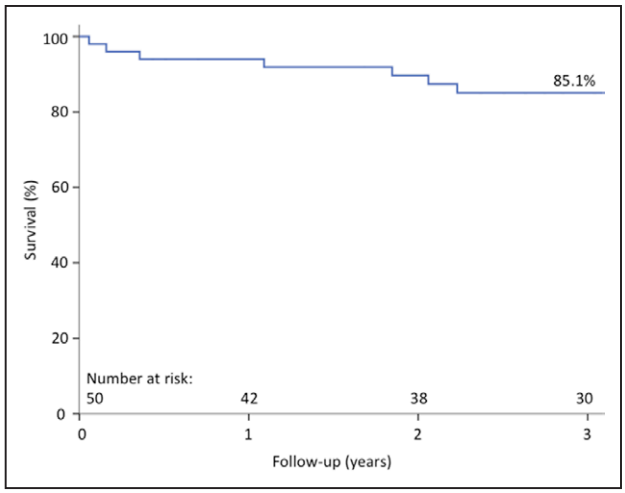

Figure 4. Kaplan–Meier curve depicting survival after redo TAVR.

Valve performance compared favorably with other recent TAVR series. Moderately elevated intraprosthetic gradients (mean gradients ≥20 mm Hg) were reported in 5 patients (10%) presenting with stenosis of the fist transcatheter valve, even though in 1 of these, patient–prosthesis mismatch was reported immediately after the first TAVR. This observation differs from valve-in-valve procedures for the treatment of degenerated surgical aortic bioprostheses, in which significantly elevated postprocedural gradients were more common (26.8%), particularly in small (<20 mm) surgical valves (41.2%) and intermediate-sized (21–22 mm) valves (35.8%).[16] The lower profile of the transcatheter valves as compared with the surgical bioprostheses is likely responsible for these more favorable hemodynamic performances. However, it must be underlined that, after redo TAVR, patients with valve degeneration had slightly higher transvalvular gradients as compared with those who had a second TAV implanted because of PVR.

The impact of this study on clinical practice is highly relevant for several reasons: first of all, although, to date, redo TAVR is an uncommon procedure, with the growing worldwide adoption of TAVR and its gradual extension to younger and lower-risk population, the volume of patients that in the future may require repeat procedures will increase exponentially; second, in contrast with redo valve surgery, which is technically challenging and carries a higher mortality and morbidity risk than the primary valve procedure,[17,18] redo TAVR seems to be safe with no increased risk of periprocedural complications. In addition, the sizing process is generally facilitated, and valve deployment is simplified by the presence of the first prosthesis, which serves as a fluoroscopic marker for the landing zone of the second valve. However, 3 main potential concerns associated with redo TAVR still remain. It is unknown whether the presence of 2 valves could affect the long-term durability of the prosthesis; possible leaflet thrombosis in bioprostheses is emerging as an important issue of TAVR.[19] In this series of patients, this was not observed (although no systematic computed tomography assessment was performed). We could speculate that patients with double valves may be more prone to develop this complication. Finally, access to the coronary arteries, particularly after implantation of 2 TAVs that extends into the ascending aorta (ie, CoreValve), needs to be carefully assessed.

Limitations

Limitations of this study include its retrospective design and the small sample size. However, to our knowledge, this is the largest multicenter study to report the outcomes of redo TAVR for the treatment of transcatheter valve failure. In addition, with the available data, we cannot make definite conclusions on the best strategies for device selection in redo TAVR procedures and on long-term survival because patient selection might have biased the excellent outcomes. Indeed, patients in severely reduced clinical condition presenting with TAV failure might not have received any interventional treatment. We cannot exclude leaflet thrombosis as a reversible cause of stenotic degeneration of some of the cases included in the study.[20] Finally, degree and completeness of clinical and echocardiographic follow-up among the entire TAVR populations

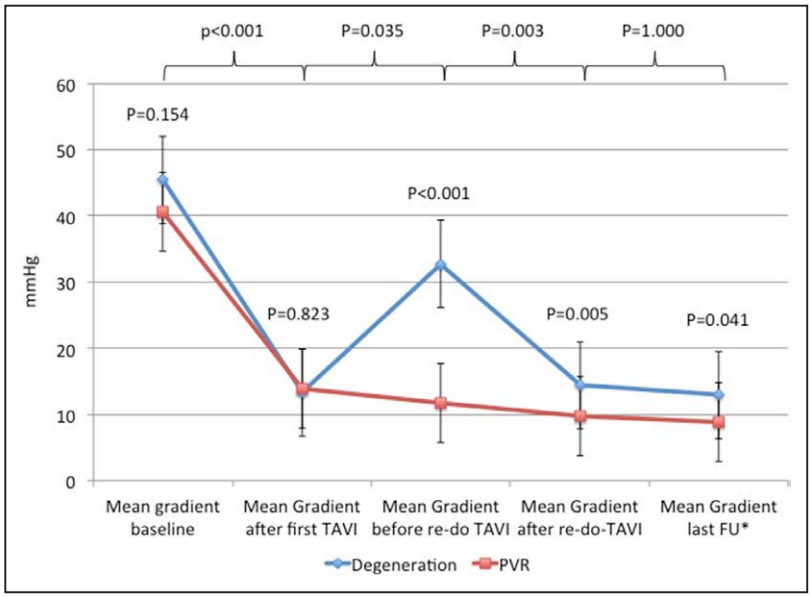

Figure 5. Transaortic gradients in patients with degenerated transcatheter aortic valve (blue line) and paravalvular regurgitation (PVR; red line). FU indicates follow-up; and TAVI, transcatheter aortic valve implantation.

Table 5. Transaortic Gradients in Patients With Failed Annular and Supra-Annular Transcatheter Aortic Valves Before and After First and Redo TAVR

	Mean Gradient Baseline, mm Hg	Mean Gradient Before First TAVR, mm Hg	Mean Gradient After First TAVR, mm Hg	Mean Gradient After Redo TAVR, mm Hg	Mean Gradient Last FU, mm Hg
Annular TAV*					
23 mm (n=6)	48.6±20	12.4±6.1	47.0±21.8	17.0±7.9	14.0±4.9
25/26 mm (n=7)	37.8±17.9	20.8±13.6	30.0±16.4	13.4±5.7	13.7±6.6
Supra-annular TAV†					
26 mm (n=10)	48.1±13.0	8.7±3.6	18.9±17.5	10.6±2.5	10.1±8.4
29 mm (n=17)	41.4±12.5	12.9±9.6	19.8±17.3	10.6±6.9	9.6±4.9
31 mm (n=11)	40.7±14.2	13.7±4.7	13.9±4.5	12.6±5.2	11.1±7.0

FU indicates follow-up; TAV, transcatheter aortic valve; and TAVR, transcatheter aortic valve replacement.
*Including Edwards SAPIEN, SAPIEN XT, SAPIEN 3, and Portico.
†Including CoreValve.

treated at each participating center is unknown, thus making impossible a precise estimate of TAV failure. However, it was not the aim of this study to assess the rate of transcatheter valve degeneration in a certain TAVR population.

Conclusions

Redo TAVR for the treatment of postprocedural and late occurrence of PVR and TAV prosthesis failure seems to be safe, and it is associated with favorable acute and midterm clinical and echocardiographic outcomes.

Disclosures

Drs Barbanti and Kapadia are consultants for Edwards Lifesciences. Dr Webb is consultant for Edwards, Medtronic, and St Jude Medical. Drs Sinning and Nickenig have received speaker honoraria and research grants from Medtronic, Edwards Lifesciences, Direct Flow Medical, and Boston Scientific. Dr Piazza is a proctor and consultant for Medtronic. Dr Van Mieghem has received research grants from Edwards Lifesciences, Medtronic, and Boston Scientific. Dr de Jaegere is a proctor for St Jude Medical and Boston Scientific. Dr Colombo is consultant for Edwards Lifesciences, a minor shareholder of Direct Flow. Dr Tchetche is proctor for Edwards Lifesciences, Medtronic, and Boston Scientific. Dr Latib serves on a Medtronic advisory board and is a consultant for Direct Flow Medical. Dr De Marco is a consultant for Direct Flow Medical. Dr Won-Keun is proctor for SJM Portico and Symetis. Dr Lange is a proctor for Medtronic and Edwards Lifesciences and has received honoraria payments. Dr Möllmann has received proctor salary or speakers' honoraria from Abbott, Medtronic, Edwards Lifesciences, St Jude Medical, and Symetis. Dr Walther has received proctor salary and speakers' honoraria from Medtronic and Symetis. Dr Dvir is consultant for Edwards Lifesciences and St Jude Medical. Dr Bleiziffer and Prof Tamburino are consultants for Medtronic and St Jude Medical. Drs Bedogni and Petronio are consultants for Medtronic. Dr Rodés-Cabau is a consultant for Edwards Lifesciences and St-Jude Medical. Dr Makkar has received grant support from Edwards Lifesciences and St Jude Medical; is a consultant for Abbott Vascular, Cordis, and Medtronic; and holds equity in Entourage Medical. Dr Svensson is a consultant for Edwards Lifesciences, holds equity in Cardiosolutions and ValvXchange, and has Intellectual Property Rights/Royalties from Posthorax. Dr Rodés-Cabau has received research grants from Edwards Lifesciences, Medtronic, and St Jude Medical. The other authors report no conflicts.

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