

# Transcatheter aortic valve implantation versus redo surgery for failing surgical aortic bioprostheses: a multicentre propensity score analysis



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## KEYWORDS

- prior cardiovascular surgery
- valve-in-valve
- valve restenosis

## Abstract

**Aims:** Transcatheter aortic valve implantation for a failing surgical bioprosthesis (TAV-in-SAV) has become an alternative for patients at high risk for redo surgical aortic valve replacement (redo-SAVR). Comparisons between these approaches are non-existent. This study aimed to compare clinical and echocardiographic outcomes of patients undergoing TAV-in-SAV versus redo-SAVR after accounting for baseline differences by propensity score matching.

**Methods and results:** Patients from seven centres in Europe and Canada who had undergone either TAV-in-SAV (n=79) or redo-SAVR (n=126) were identified. Significant independent predictors used for propensity scoring were age, NYHA functional class, number of prior cardiac surgeries, urgent procedure, pulmonary hypertension, and COPD grade. Using a calliper range of  $\pm 0.05$ , a total of 78 well-matched patient pairs were found. All-cause mortality was similar between groups at 30 days (6.4% redo-SAVR vs. 3.9% TAV-in-SAV; p=0.49) and one year (13.1% redo-SAVR vs. 12.3% TAV-in-SAV; p=0.80). Both groups also showed similar incidences of stroke (0% redo-SAVR vs. 1.3% TAV-in-SAV; p=1.0) and new pacemaker implantation (10.3% redo-SAVR vs. 10.3% TAV-in-SAV; p=1.0). The incidence of acute kidney injury requiring dialysis was numerically lower in the TAV-in-SAV group (11.5% redo-SAVR vs. 3.8% TAV-in-SAV; p=0.13). The TAV-in-SAV group had a significantly shorter median total hospital stay (12 days redo-SAVR vs. 9 days TAV-in-SAV; p=0.001).

**Conclusions:** Patients with aortic bioprosthesis failure treated with either redo-SAVR or TAV-in-SAV have similar 30-day and one-year clinical outcomes.

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## Abbreviations

<b>COPD</b>	chronic obstructive pulmonary disease
<b>eGFR</b>	estimated glomerular filtration rate
<b>EuroSCORE</b>	European System for Cardiac Operative Risk Evaluation
<b>LVEF</b>	left ventricular ejection fraction
<b>NYHA</b>	New York Heart Association
<b>PCI</b>	percutaneous coronary intervention
<b>PS</b>	propensity score
<b>SAVR</b>	surgical aortic valve replacement
<b>STS</b>	Society of Thoracic Surgeons
<b>TAV-in-SAV</b>	transcatheter aortic valve in surgical aortic valve
<b>THV</b>	transcatheter heart valve
<b>VARC</b>	Valve Academic Research Consortium

## Introduction

Transcatheter aortic valve implantation in a failing surgical aortic valve (TAV-in-SAV) was first reported in 2007 in an elderly patient with multiple comorbidities and at extreme risk for redo surgery<sup>1</sup>. Since then, numerous small TAV-in-SAV case series have demonstrated good results with this procedure, with 30-day risk of mortality ranging from 0% to 7.4%<sup>2-4</sup>.

The historical gold standard treatment for patients with a failing surgical bioprosthesis is redo-SAVR. Although the clinical outcomes of redo-SAVR approach those of the index procedure in low-risk patients, periprocedural mortality rates increase significantly in those at high risk, with in-hospital mortality ranging from 2.3 to 16.4%<sup>5-7</sup>. This is especially true in the elderly as the odds ratio of mortality for redo-SAVR is 1.49 (1.10-1.97) per decade<sup>6</sup>. TAV-in-SAV is a less invasive procedure that obviates the need for sternotomy and cardiopulmonary bypass, and eliminates the risk of injury to a substernal internal mammary arterial graft in patients with previous coronary artery bypass grafting (CABG).

Recently, a 459-patient TAV-in-SAV registry<sup>8</sup> reported 30-day and one-year mortality rates of 7.6% and 16.8%, respectively. Of note, moderately elevated post-procedural mean gradients >20 mmHg were reported in 27% of patients. In March 2015, the FDA approved the Medtronic CoreValve<sup>®</sup> (Medtronic, Minneapolis, MN, USA) for the treatment of a failing surgical bioprosthesis in high/extreme surgical risk patients. In October 2015, the Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) received the same approval.

Studies comparing matched patients undergoing redo-SAVR or TAV-in-SAV are currently inexistent. While observational case series suggest similar clinical outcomes between the two approaches, patient characteristics are often dissimilar, making any comparison difficult and possibly futile<sup>8,9</sup>. Adequately powered prospective randomised trials are unlikely given the sample size requirements in this very specific subgroup of patients<sup>10</sup>.

To investigate the comparative clinical effectiveness between TAV-in-SAV and redo-SAVR, we conducted a propensity score-matched

analysis across seven international centres. Results from this study could validate the use of TAV-in-SAV as an alternative to redo-SAVR.

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## Methods

### PATIENT SELECTION AND IDENTIFICATION OF THE STUDY POPULATION

Patients were eligible for study inclusion if they had undergone TAV-in-SAV or redo-SAVR for a failing aortic bioprosthesis (stenosis, regurgitation or both) between January 2007 and January 2015 in one of seven centres in Europe and Canada: Antwerp University Hospital, Antwerp, Belgium; Ferrarotto Alessi Hospital, Catania, Italy; German Heart Centre, Munich, Germany; Lille University Health Centre, Lille, France; Rigshospitalet, Copenhagen, Denmark; Royal Victoria Hospital, Montreal, Canada; and Universitätsklinikum Bonn, Bonn, Germany. All patients were identified by retrospective assessment of institutional databases. The selection of patients for TAV-in-SAV or redo-SAVR was performed at an institutional level, following consideration of the risk profile of each case and Heart Team assessment. For all patients, centres submitted a dedicated case report form detailing patient baseline characteristics, echocardiographic data, procedural information and scheduled clinical follow-up.

The study included all consecutive patients who were potential candidates for either a TAV-in-SAV or redo-SAVR. Patients were excluded if they underwent redo-SAVR for paravalvular leak, valve thrombosis or endocarditis. Concomitant coronary revascularisation performed by either percutaneous or surgical techniques was permitted. Local ethics committees approved the retrospective collection of data, and all subjects gave written informed consent for their intervention.

### DATA COLLECTION AND STUDY ENDPOINTS

Baseline data were complete for all patients, except logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) and STS scores which were unavailable in 35% of redo-SAVR patients. The primary endpoint was 30-day mortality. Secondary endpoints included one-year mortality, stroke, myocardial infarction, new pacemaker implantation, acute kidney injury requiring dialysis, post-procedural mean gradient, and length of hospital stay. Endpoints were defined according to the updated Valve Academic Research Consortium (VARC) criteria<sup>11</sup>. Pulmonary hypertension was defined as systolic pulmonary artery pressure above 50 mmHg as estimated by tricuspid regurgitation jet on Doppler echocardiography. Procedure urgency was defined as being performed in a hospitalised patient rather than electively.

### STATISTICAL ANALYSIS

Baseline clinical and surgical characteristics were compared using Fisher's exact test for categorical variables and the Student's t-test for continuous variables. Propensity scores were derived by including age and sex with pre-treatment variables that were independently associated with treatment selection at  $p < 0.10$  in a multivariable model of all variables. Propensity scores among patients undergoing either TAV-in-SAV or redo-SAVR were then matched using a calliper

range of  $\pm 0.05$  to obtain matched pairs of patients. Replacements were permitted (maximum of four uses) in the redo-SAVR group.

In addition to matching, we also compared redo-SAVR and TAV-in-SAV using the inverse probability of treatment weights technique. Patients with propensity scores below the 2.5<sup>th</sup> percentile in the TAV-in-SAV group and above the 97.5<sup>th</sup> percentile in the redo-SAVR group were removed. Next, a weight was attributed to each remaining patient according to the inverse of their propensity score, and comparisons were performed on this weighted and trimmed data set.

Survival at 30 days and one year was plotted using Kaplan-Meier curves and between group differences were calculated using the log-rank test. A p-value  $< 0.05$  was considered significant. Statistical analyses were performed with SPSS, Version 23 (IBM Corp., Armonk, NY, USA).

## Results

### BASELINE CHARACTERISTICS

A total of 205 consecutive patients meeting inclusion and exclusion criteria underwent redo-SAVR (n=126) or TAV-in-SAV (n=79)

for a failing aortic bioprosthesis during the study period. Patients undergoing TAV-in-SAV were older, more likely to have had multiple prior cardiac surgeries, be in NYHA functional Class III or IV, have higher logistic EuroSCORE and STS scores, and display more comorbidities (Table 1).

Standardised differences between groups after trimming and weighting were less than 0.20 (i.e., small) for all variables except atrial fibrillation and number of previous surgeries (Table 1).

### PROPENSITY SCORE MATCHING

Pre-treatment variables found to be independent predictors of treatment selection and used for propensity scoring were age, NYHA functional class, number of prior cardiac surgeries, urgent procedure, pulmonary hypertension, and chronic obstructive pulmonary disease (COPD) grade (Table 2). These variables were all associated with assignment to TAV-in-SAV, with the exception of urgent procedure, which was associated with redo-SAVR.

Propensity score matching generated 78 pairs of patients. Baseline characteristics were similar between groups after propensity

**Table 1. Baseline characteristics: before vs. after PS matching and standardised differences.**

Variable	Before PS matching				After PS matching				IPTW		
	Redo-SAVR (n=126)	TAV-in-SAV (n=79)	Diff	p-value	Redo-SAVR (n=78)	TAV-in-SAV (n=78)	Diff	p-value	Diff	p-value	
Age	67.6 $\pm$ 12.9	78.1 $\pm$ 8.0	-0.98	<0.001	77.4 $\pm$ 5.0	78.0 $\pm$ 8.0	-0.09	0.58	0.19	0.1	
Female sex	46 (37)	39 (49)	-0.26	0.08	34 (44)	39 (50)	-0.13	0.52	-0.11	0.4	
Logistic EuroSCORE	14.0 $\pm$ 12.4	22.0 $\pm$ 16.0	-0.56	<0.001	22.1 $\pm$ 18.3	22.1 $\pm$ 16.0	0.00	0.99	-0.01	0.92	
STS score*	4.4 $\pm$ 4.4	7.4 $\pm$ 4.9	-0.64	<0.001	5.8 $\pm$ 4.6	7.2 $\pm$ 4.9	-0.29	0.09	-0.07	0.62	
More than 1 prior cardiac surgery	7 (6)	11 (14)	-0.29	0.05	9 (12)	10 (13)	-0.04	0.81	0.28	0.03	
NYHA	I	9 (8)	1 (1)	0.30	0.05	1 (1)	1 (1)	0.00	0.16	-0.14	0.32
	II	33 (28)	14 (18)	0.21		8 (11)	13 (17)	-0.19		0.01	1
	III	53 (45)	42 (54)	-0.22		33 (45)	42 (55)	-0.23		0.06	0.71
	IV	22 (19)	21 (27)	-0.22		32 (43)	21 (27)	0.30		-0.04	0.79
Urgent procedure	17 (14)	5 (6)	0.24	0.16	10 (13)	5 (6)	0.22	0.28	0.08	0.55	
LVEF (%)	50.6 $\pm$ 13.3	50.7 $\pm$ 13.4	-0.01	0.96	49.5 $\pm$ 13.4	50.7 $\pm$ 13.5	-0.09	0.58	0.02	0.87	
Atrial arrhythmia (flutter or fibrillation)	39 (31)	27 (34)	-0.07	0.65	29 (37)	27 (35)	0.05	0.87	-0.25	0.04	
Diabetes mellitus	15 (12)	16 (20)	-0.23	0.11	12 (15)	15 (19)	-0.10	0.67	-0.02	0.87	
Hypertension	80 (64)	57 (72)	-0.19	0.23	57 (73)	56 (72)	0.03	1	-0.11	0.43	
Coronary artery disease necessitating revascularisation	34 (27)	34 (43)	-0.34	0.02	25 (32)	33 (42)	-0.21	0.25	-0.02	0.9	
Prior CABG	26 (21)	25 (32)	-0.25	0.1	18 (23)	24 (31)	-0.17	0.37	0.08	0.59	
Prior stroke	15 (12)	7 (9)	0.10	0.64	9 (12)	7 (9)	0.08	0.79	-0.09	0.55	
Peripheral vascular disease	13 (10)	12 (15)	-0.15	0.38	13 (17)	11 (14)	0.07	0.83	-0.14	0.29	
COPD	None	116 (92)	63 (80)	0.36	0.04	70 (90)	62 (80)	0.29	0.15	-0.03	0.86
	Grade 1	4 (3)	7 (9)	-0.24		2 (3)	7 (9)	-0.28		0.18	0.18
	Grade 2 or more	6 (5)	9 (11)	-0.25		6 (8)	9 (12)	-0.13		-0.11	0.38
Pulmonary hypertension	13 (10)	24 (30)	-0.51	0.001	28 (36)	24 (31)	0.11	0.61	-0.05	0.77	
eGFR (ml/min/1.73 m <sup>2</sup> )	70.2 $\pm$ 22.8	59.7 $\pm$ 18.0	0.51	<0.001	59.3 $\pm$ 20.7	59.7 $\pm$ 18.2	-0.02	0.89	-0.1	0.37	

Values are mean $\pm$ SD or n (%). \*STS score was available for 80 patients in the redo-SAVR group before PS matching and 51 patients after PS matching. CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; Diff: standardised difference; eGFR: glomerular filtration rate estimated by the MDRD formula; EuroSCORE: European System for Cardiac Operative Risk Evaluation; IPTW: inverse probability treatment weighting after trimming of 2.5% of tails; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association (functional class); PS: propensity score; SAVR: surgical aortic valve replacement; STS: Society of Thoracic Surgeons; TAV-in-SAV: transcatheter aortic valve in surgical aortic valve

matching (Table 1). In each pair, redo-SAVR occurred at a median of 421 days before TAV-in-SAV. However, in 28 of 78 pairs, TAV-in-SAV predated redo-SAVR.

**Table 2. Independent predictors of treatment assignment.**

Variable	OR	p-value
Age (per 1-year increment)	1.128	<0.0001
NYHA class (per 1 class increment)	1.553	0.06
Number of prior surgeries (per surgery)	4.704	0.008
Urgent procedure	0.218	0.02
Pulmonary hypertension	2.059	0.1
COPD grade (per 1 grade increment)	1.469	0.1

Odds ratios (OR) values above 1 indicate association with TAV-in-SAV. COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association

The surgical and bioprosthesis characteristics of matched patients are displayed in Table 3. The mean delay between index procedure and either redo-SAVR or TAV-in-SAV was 8.2 and 9 years, respectively (p=0.30). This delay was less than three years in 16.4% of the total population, with regurgitation being the most common mode of failure in this “accelerated failure” subgroup. While pure regurgitation was the mode of failure in half the patients in the redo-SAVR group (50.0%), pure stenosis was the most common mode of failure in TAV-in-SAV patients (51.3%). In total, 25 patients in the redo-SAVR group (32%) had coronary artery disease (CAD) necessitating revascularisation. Of these, 21 underwent concomitant CABG at the time of surgery; the other four underwent PCI as conduits for bypass were unavailable. In the TAV-in-SAV group, 33 patients (42%) had CAD necessitating revascularisation (p=0.25 vs. redo-SAVR group). PCI was performed before TAV-in-SAV in 32 patients, and at the time of procedure in one patient. A Carpentier-Edwards (Edwards Lifesciences) was the failing bioprosthesis in 19 patients of the redo-SAVR group (24.4%) and 34 patients of the TAV-in-SAV group (43.6%). Other valves were found less frequently. Types and sizes of surgical bioprostheses or transcatheter heart valves (THV) used in both groups are also displayed in Table 3. Among patients undergoing TAV-in-SAV, self-expanding and balloon-expandable THV were used in similar proportions, and transfemoral access was chosen in 53.8% of patients. Conversion to open surgery did not occur in any of the TAV-in-SAV patients, and requirement for a second THV during the procedure occurred in four (5.1%) cases.

**CLINICAL OUTCOMES**

Table 4 describes clinical outcomes at 30 days and one year for both groups before and after propensity score matching. Time-to-event curves comparing both treatment modalities after matching are depicted in Figure 1. Thirty-day follow-up was complete in 99.4%, and 88.5% at one year. Thirty-day Kaplan-Meier mortality was 2.5% higher in the redo-SAVR group compared to the TAV-in-SAV group, but this difference did not reach statistical significance (6.4 vs. 3.9%, respectively; p=0.49). One-year mortality was similar between groups (13.1 redo-SAVR vs. 12.3% TAV-in-SAV; p=0.80). Similar results were found when using inverse probability of treatment weights (Table 5).

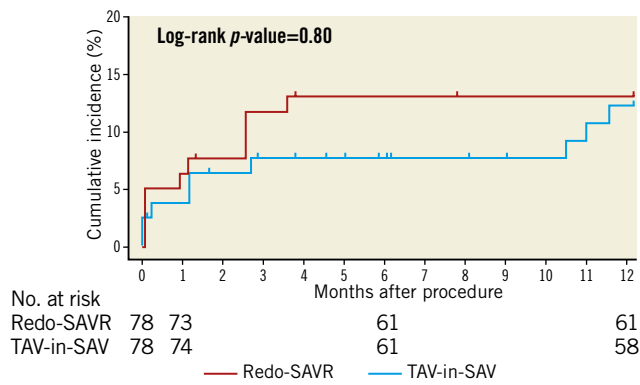
**Table 3. Procedural and bioprosthesis characteristics of PS-matched patients.**

Variable		Redo-SAVR (n=78)	TAV-in-SAV (n=78)	p-value
Time since last SAVR (years)		8.2±5.1	9.0±4.3	0.3
Type of failing bioprosthesis	Stented	60 (78)	65 (83)	0.68
	Stentless	17 (22)	13 (17)	
Label size of failing bioprosthesis	≤21 mm	32 (41)	18 (23)	<0.0001
	>21 mm and <25 mm	14 (18)	40 (51)	
	≥25 mm	19 (24)	17 (22)	
	Unknown	13 (17)	3 (4)	
Mechanism of failure	Stenosis	24 (31)	40 (51)	0.001
	Regurgitation	39 (50)	17 (22)	
	Mixed	15 (19)	21 (27)	
Centre	Munich	23 (30)	33 (42)	0.1
	Copenhagen	19 (24)	11 (14)	
	Bonn	16 (21)	11 (14)	
	Lille	7 (9)	6 (8)	
	Montreal	8 (10)	4 (5)	
	Catania	4 (5)	7 (9)	
	Antwerp	1 (1)	6 (8)	
Type of bioprosthesis used for redo-SAVR	Stented	77 (99)		
	Stentless	1 (1)		
Label size	≤21 mm	48 (62)		
	>21 mm and <25 mm	16 (21)		
	≥25 mm	15 (19)		
THV type	CoreValve		46 (59)	
	Edwards (SAPIEN/XT/SAPIEN 3)		32 (41)	
THV size	23		45 (58)	
	26		26 (33)	
	29		4 (5)	
	31		3 (4)	
THV access site	Transfemoral		42 (54)	
	Transapical		24 (31)	
	Other		12 (15)	
Conversion to open surgery			0 (0)	
Requirement for a second THV			4 (5)	

Values are mean±SD or n (%). PS: propensity score; SAVR: surgical aortic valve replacement; TAV-in-SAV: transcatheter aortic valve in surgical aortic valve; THV: transcatheter heart valve

**VALVE TYPES**

Kaplan-Meier curves of one-year mortality according to failing surgical bioprosthesis type are shown in Figure 2. Mortality was significantly higher in patients undergoing TAV-in-SAV for a failing stentless bioprosthesis as compared to redo-SAVR (32.7 vs. 0%, p=0.01). For patients with a failing stented bioprosthesis, mortality rates were lower with TAV-in-SAV compared to redo-SAVR, but this failed to reach statistical significance (8.3 vs. 17.2%, p=0.12). Mortality rates were similar between groups

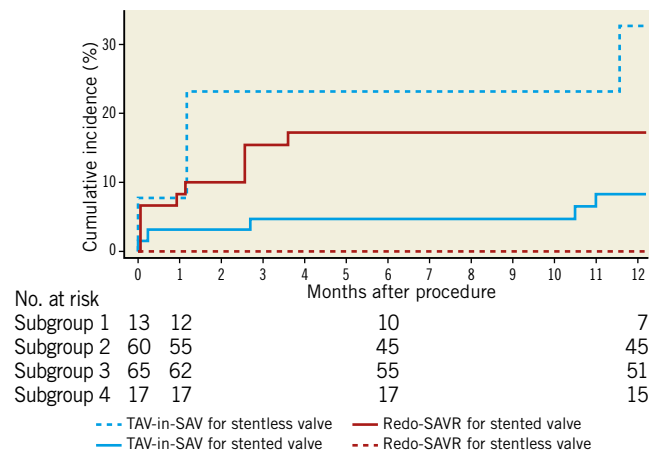


**Figure 1.** Cumulative incidence of all-cause mortality. Cumulative incidence (%) of all-cause one-year mortality in redo-SAVR (red line) and TAV-in-SAV (blue line). There was no difference in one-year mortality between groups.

when stratified by failure mechanism and failing prosthesis size. There was no difference in 30-day mortality between patients who underwent TAV-in-SAV with the Edwards THV compared to those who underwent TAV-in-SAV with the Medtronic CoreValve THV (3.1 vs. 4.3%, respectively;  $p=0.77$ ).

## SECONDARY OUTCOME MEASURES

Propensity-matched groups did not differ with respect to the following clinical outcomes: stroke, myocardial infarction and new pacemaker implantation. Patients with a failing stentless bioprosthesis had a higher rate of new pacemaker implantation compared to those with a stented bioprosthesis, regardless of treatment modality (23.3 vs. 6.4%;  $p=0.01$ ). There was three times more renal failure requiring dialysis in the redo-SAVR group compared to the TAV-in-SAV group; however, this difference did not reach statistical significance (11.5% vs. 3.8%, respectively;  $p=0.13$ ). Median total hospital length of stay was three days shorter in



**Figure 2.** Cumulative incidence of all-cause mortality stratified by failing bioprosthesis type. Cumulative incidence (%) of all-cause one-year mortality in TAV-in-SAV for failing stentless valve (group 1, dashed blue line), redo-SAVR for failing stented valve (group 2, solid red line), TAV-in-SAV for failing stented valve (group 3, solid blue line), and redo-SAVR for failing stentless valve (group 4, dashed red line). There was a statistically significant difference in one-year mortality between groups 1 and 4.

the TAV-in-SAV than in the redo-SAVR group (9 vs. 12 days,  $p=0.001$ ) (Table 4). Similar results were found when using inverse probability of treatment weights (Table 5).

## ECHOCARDIOGRAPHIC OUTCOMES

At 30 days, redo-SAVR was associated with a lower mean gradient compared to TAV-in-SAV (14.3 mmHg vs. 18.1 mmHg,  $p=0.01$ ). This difference was due to a significantly higher mean gradient in the Edwards TAV-in-SAV group (21.3±7.2 mmHg) compared to patients in the CoreValve TAV-in-SAV group (15.4±6.7 mmHg) and the redo-SAVR group (14.3±6.2 mmHg) (Figure 3A). This

**Table 4.** Thirty-day and one-year outcomes before and after PS matching.

Variable	Before PS matching			After PS matching			
	Redo-SAVR (n=126)	TAV-in-SAV (n=79)	p-value	Redo-SAVR (n=78)	TAV-in-SAV (n=78)	OR or coefficient (95% CI)	p-value
Thirty-day outcomes							
Death	6 (4.8)	3 (3.8)	1	5 (6.4)	3 (3.9)	0.58 (0.13-2.53)	0.49
Stroke	2 (1.6)	1 (1.3)	1	0 (0)	1 (1)	3.04 (0.12-75.75)	1
Myocardial infarction	2 (1.6)	1 (1.3)	1	0 (0)	1 (2)	3.04 (0.12-75.75)	0.49
Renal failure requiring dialysis	8 (6.3)	3 (3.8)	0.54	9 (12)	3 (4)	0.31 (0.08-1.18)	0.13
New pacemaker implantation	11 (8.7)	9 (11.4)	0.63	8 (10)	8 (10)	1.00 (0.36-2.81)	1
Mean gradient (mmHg)	14.2±5.9	18.1±7.4	0.002	14.3±6.2	18.1±7.4	+3.78 (0.95-6.60)	0.01
Mean gradient greater than 20 mmHg	9 (16.4)	20 (34.5)	0.03	7 (17)	21 (36)	3.74 (1.48-9.41)	0.04
Total hospital length of stay (median [IQR])	12 (8-18.5)	9 (6.75-13)	0.002	12 (8-24)	9 (7-13)	-9.38 (-14.84, -3.92)	0.001
One-year mortality	15 (12.2)	10 (13.5)	0.82	10 (13.1)	9 (12.3)	0.89 (0.34-2.32)	0.80

Values are mean±SD or n (%) unless specified otherwise. IQR: interquartile range; PS: propensity score; SAVR: surgical aortic valve replacement; TAV-in-SAV: transcatheter aortic valve in surgical aortic valve



**Table 5. Thirty-day and one-year outcome comparisons of TAV-in-SAV vs. redo-SAVR (trimmed groups, inverse probability of treatment weights).**

Variable	OR or coefficient (95% CI)	p-value
Thirty-day outcomes		
Death	0.98 (0.12-8.40)	0.99
Stroke	2.18 (0.13-35.70)	0.59
Myocardial infarction	2.51 (0.15-41.20)	0.52
Renal failure requiring dialysis	1.21 (0.24-6.11)	0.82
New pacemaker implantation	0.99 (0.31-3.15)	0.99
Mean gradient (mmHg)	+5.37 (2.49-8.26)	<0.001
Mean gradient greater than 20 mmHg	6.70 (1.37-32.70)	0.02
Total hospital length of stay (days)	-4.59 (-10.15, -0.97)	0.11
One-year mortality	0.74 (0.24-2.31)	0.61
Odds ratios and continuous coefficients use redo-SAVR as reference group. SAVR: surgical aortic valve replacement; TAV-in SAV: transcatheter aortic valve in surgical aortic valve		

difference between devices was found regardless of failing device inner diameter (**Figure 3B**). Furthermore, post-procedural transaortic gradients >20 mmHg were more than twice as likely in the Edwards TAV-in-SAV group (51.9%) compared to the CoreValve TAV-in-SAV and redo-SAVR groups (22.6 and 17.1%, respectively). **Figure 3C** displays mean post-procedural gradients stratified according to the type of failing bioprosthesis. Independent predictors of higher post-procedural gradients were a failing stented bioprosthesis (increase of 2.5 mmHg;  $p=0.02$ ), treatment with an Edwards THV (increase of 4.7 mmHg compared to redo-SAVR and 4.3 mmHg compared to CoreValve; both  $p<0.01$ ), and lower EuroSCORE (increase of 0.31 mmHg per 5% decrease in EuroSCORE;  $p=0.02$ ).

## Discussion

The major findings of this propensity-matched comparison of redo-SAVR and TAV-in-SAV for failing aortic bioprostheses are as follows: 1) redo-SAVR and TAV-in-SAV for a failing bioprosthesis showed similar rates of 30-day and one-year mortality; 2) total hospital length of stay was shorter with TAV-in-SAV than redo-SAVR; 3) mean post-procedural gradients were higher with Edwards TAV-in-SAV compared to redo-SAVR and CoreValve TAV-in-SAV; and 4) failing stentless bioprostheses were associated with a higher rate of new pacemaker implantation and a lower mean post-procedural gradient, regardless of treatment modality.

Mortality rates of 3.9% at 30 days for TAV-in-SAV are nearly two times lower than those reported in other studies<sup>3,12</sup>. The Valve-in-Valve registry reported a 30-day mortality rate of 7.6% in patients with a similar risk profile<sup>8</sup>. This may be due to site selection bias, as we included only high-volume centres in the present study. While smaller valve sizes and valve stenosis were shown to be associated with higher mortality rates in the Valve-in-Valve registry, this was not found to be the case in our study.

With respect to the surgical group, the 6.4% and 13.1% mortality rates at 30 days and one year, respectively, are comparable to those reported in the surgical literature. Jones et al reported a 30-day mortality rate of 6.4% in an all-comers series<sup>6</sup>. Eitz et al reported 30-day and one-year mortality rates of 16.4% and 23%, respectively, in a cohort of 71 octogenarians<sup>5</sup>. However, comparisons to this last series may be inappropriate because patients with emergent indications such as endocarditis and thrombosis were excluded from our study.

The higher mortality rates with TAV-in-SAV in patients with a failing stentless bioprosthesis should be treated with circumspection as they are based on only four events in a small subgroup. Only one death occurred in the first 30 days, indicating that mortality may be due to patient characteristics more than procedural failure.

The main advantage of stentless bioprostheses over stented valves seems to be the superior haemodynamic profile achieved after the procedure with lower mean gradients. This is due to the increased space in the aortic root of patients with stentless valves.

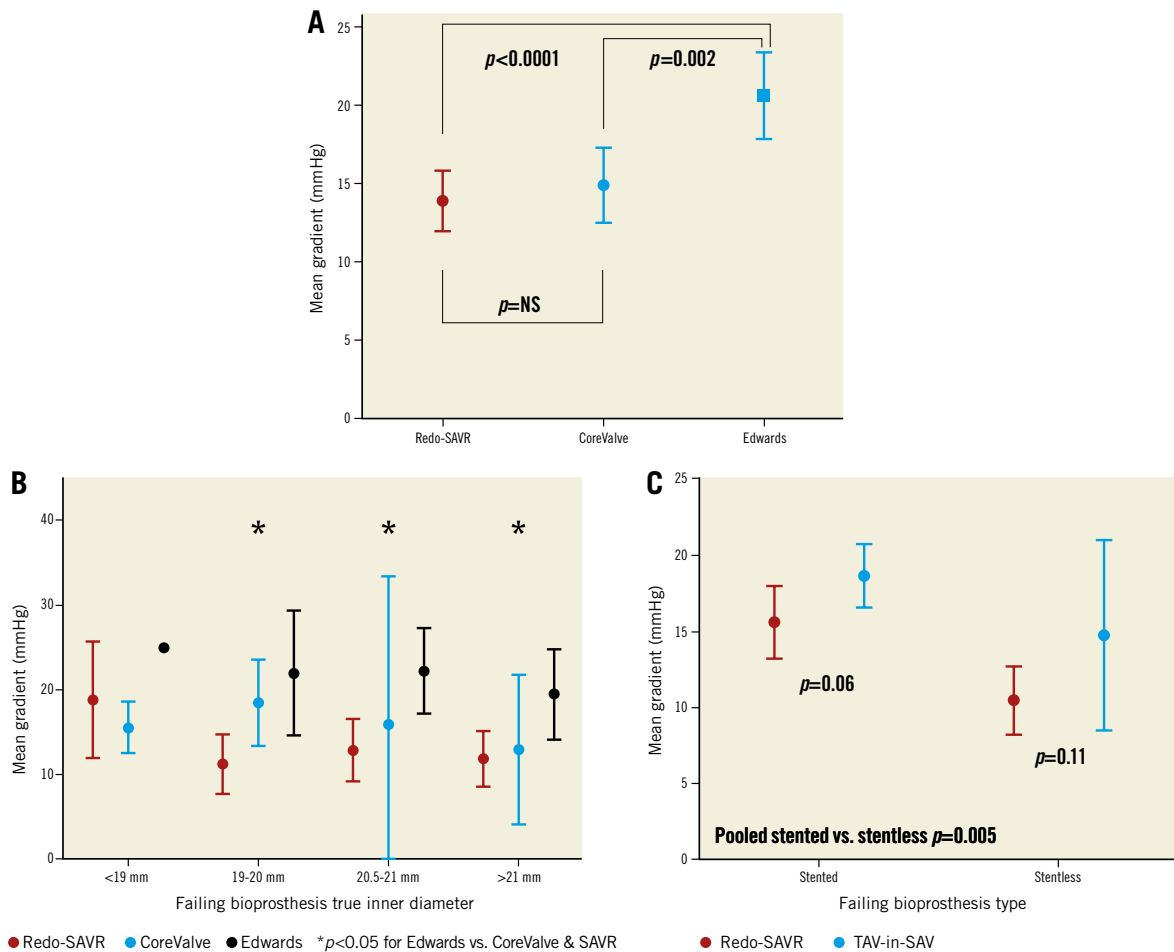
Redo-SAVR also allows increased space in the aortic root compared to TAV-in-SAV. However, the CoreValve bioprosthesis, with its supra-annular leaflet position, yielded similar post-procedural gradients to redo-SAVR, while the Edwards THV (intra-annular leaflets) produced higher gradients, regardless of failing device size<sup>13</sup>. The CoreValve device may be better suited to tackle TAV-in-SAV but, in our study, higher mean gradients did not seem to translate into midterm clinical events.

There was no difference between TAV-in-SAV and redo-SAVR with respect to other clinical outcomes. The rate of renal failure requiring dialysis was numerically higher in the redo-SAVR group, but statistical significance was not found, possibly because of lack of power. The similar outcomes regarding pacemakers (something which is different from the literature concerning procedures performed on the native aortic valve) may be due to the more extensive debridement involving the ventricular septum in redo-SAVR (thereby increasing the pacemaker rate in that group) and the relative “shielding” of the septum by the failing prosthesis stent for TAV-in-SAV (thereby decreasing the pacemaker rate in that group). The relatively high rate of new pacemaker implantation in the stentless bioprosthesis group undergoing TAV-in-SAV may be related to baseline conduction disturbances, the absence of “shielding”, and deeper than usual implantation in these challenging cases.

As reported in previous comparisons between TAVR and SAVR, less invasive approaches are associated with shorter durations of hospital stay<sup>14</sup>. Total duration of hospital stay was similar to those reported in the PARTNER A trial.

## Limitations

The present study has limitations inherent to all retrospective analyses. First, reasons for treatment allocation cannot be fully resolved, despite attempts for propensity matching. The large residual standardised differences after PS matching are a possible marker of residual confounding. Certain baseline characteristics, such as failing bioprosthesis size and mechanism of



**Figure 3.** In-hospital mean gradient by treatment type. *A*) Post-procedural mean aortic gradient for patients in the redo-SAVR group (red circle), CoreValve TAV-in-SAV group (blue circle), and Edwards TAV-in-SAV group (blue square). Error bars represent 95% confidence interval. *B*) In-hospital mean gradient stratified by failing bioprosthesis true inner diameter and replacement device. P-values are for comparisons between Edwards (black) and redo-SAVR grouped with CoreValve (red and blue) for each size. Error bars represent 95% confidence interval. Only one case was performed with the Edwards device for the smallest size (<19 mm). *C*) In-hospital mean gradient stratified by failing bioprosthesis type. Post-procedural mean aortic gradient for patients with a failing stented bioprosthesis (left) and a failing stentless bioprosthesis (right). P-values are for comparisons between redo-SAVR (red) and TAV-in-SAV (blue). Error bars represent 95% confidence interval. The difference in gradients for pooled stented vs. stentless bioprostheses was statistically significant ( $p=0.005$ ).

failure, were dissimilar. Both of these are proven to be related to better outcomes in TAV-in-SAV. On the other hand, STS scores may appear to favour redo-SAVR. In this context, the direction and magnitude of bias cannot be determined. Matching for bioprosthesis would have been ideal, but impractical because the number of matched pairs would decrease. Smaller valves were treated more often by redo-SAVR because there are fewer transcatheter devices available for small surgical valves (for example, for a 19 mm Carpentier-Edwards SAV, only the Edwards SAPIEN 20 mm is recommended). Including more patients from more centres would not, in our view, modify the proportions of small surgical valves treated by redo-SAVR or TAV-in-SAV. With respect to revascularisation, groups differ because PCI was undertaken before the procedure in the TAV-in-SAV group, rather than during the procedure, as in redo-SAVR. Sites decided

to perform PCI before TAV-in-SAV or CABG during redo-SAVR based on different criteria and did not report this in the same manner. Therefore, adjustment for this variable could not be performed. This retrospective trial used data that were not audited, and the collected haemodynamic data were not core laboratory adjudicated. STS scores were not available for a significant proportion of surgical patients. However, most of the elements that make up the STS score were not missing and fairly well balanced after matching. We preferred not to calculate missing STS scores with the data at hand, as these calculated “*post hoc*” values would be biased by the use of a calculator version that does not match the date of the procedure, giving artefactually low values<sup>15</sup>. In addition, the logistic EuroSCORE was almost identical between groups after matching. Follow-up was limited to one year, limiting the long-term assessment of haemodynamic

findings. However, results up to one year are the current standard in studies focused on the elderly (mean age >77 years in each group) undergoing this type of procedure. Large randomised controlled trials would palliate most of these limitations. Realistically, as these are relatively infrequent procedures, we may never see an adequately powered randomised trial.

## Conclusions

Patients with aortic bioprosthesis failure treated with either redo-SAVR or TAV-in-SAV have similar 30-day and one-year clinical outcomes.

### Impact on daily practice

Patients with a failing aortic bioprosthesis at high risk for redo surgery have similar outcomes whether they undergo TAV-in-SAV or redo-SAVR.

### Conflict of interest statement

D. Mylotte, L. Søndergaard, J. Bosmans, T. Modine, J-M. Sinning, E. Grube, G. Nickenig, F. Mellert, S. Bleiziffer, R. Lange, G. Martucci, and N. Piazza report being proctor and/or consultant for Medtronic. O. De Backer, L. Søndergaard, and N. Piazza report being proctor and/or consultant for St. Jude Medical. L. Søndergaard, T. Modine, J-M. Sinning, E. Grube, G. Nickenig, and F. Mellert report being proctor and/or consultant for Boston Scientific. L. Søndergaard, M. Barbanti, J-M. Sinning, G. Nickenig, and F. Mellert report being proctor and/or consultant for Edwards Lifesciences. T. Modine reports being proctor and/or consultant for General Electric. The other authors have no conflicts of interest to declare.

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