Redo aortic valve replacement *versus* valve-in-valve trans-catheter aortic valve implantation: a UK propensity-matched analysis

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Abstract

This study sought to compare the morbidity and mortality of redo aortic valve replacement (redo-AVR) *versus* valve-in-valve trans-catheter aortic valve implantation (valve-in-valve TAVI) for patients with a failing bioprosthetic valve. A multicenter UK retrospective study of redo-AVR or valve-in-valve TAVI for patients referred for redo aortic valve intervention due to a degenerated aortic bioprosthesis. Propensity score matching was performed for confounding factors. From July 2005 to April 2021, 911 patients underwent redo-AVR and 411 patients underwent valve-in-valve TAVI. There were 125 pairs for analysis after propensity score matching. The mean age was 75.2±8.5 years. In-hospital mortality was 7.2% (n=9) for redo-AVR *versus* 0 for valve-in-valve TAVI, p=0.002. Surgical patients suffered more post-operative complications, including intra-aortic balloon pump support (p=0.02), early re-operation (p<0.001), arrhythmias (p<0.001), respiratory and neurological complications (p=0.02 and p=0.03) and multi-organ failure (p=0.01). The valve-in-valve TAVI group had a shorter intensive care unit and hospital stay (p<0.001 for both). However, moderate aortic regurgitation at discharge and higher post-procedural gradients were more common after valve-in-valve TAVI (p<0.001 for both). Survival probabilities in patients who were successfully discharged from the hospital were similar after valve-

in-valve TAVI and redo-AVR over the 6-year follow-up (log-rank p=0.26). In elderly patients with a degenerated aortic bioprosthesis, valve-in-valve TAVI provides better early outcomes as opposed to redo-AVR, although there was no difference in mid-term survival in patients successfully discharged from the hospital.

• What is already known on this topic?

Redo cardiac surgery in patients with prosthetic valve dysfunction carries a mortality rate of 5-26%; hence, a lower-risk, less-invasive percutaneous approach seems appealing. Nevertheless, patients with previous cardiac surgery have often been excluded from consideration of trans-catheter aortic valve implantation (TAVI) because of the risk of prosthetic displacement and coronary graft occlusion. Several studies report the feasibility of valve-in-valve TAVI compared with redo-aortic valve replacement (AVR) for severe bioprosthetic aortic valve dysfunction, but mid- and long-term results are limited and patient cohorts are small.

• What this study adds

This study sought to compare the outcomes of redo aortic valve replacement and valve-in-valve TAVI for patients with a failing bioprosthetic valve across the United Kingdom.

• How this study might affect research practice, or policy

In elderly patients with a degenerated aortic bioprosthesis, valve-in-valve TAVI provides better early outcomes as opposed to redo surgical AVR, although there was no difference in mid-term survival in patients successfully discharged from the hospital. Such a conclusion provides further evidence for the multi-disciplinary management of this category of patients.

Introduction

Severe aortic stenosis is an ever-growing healthcare reality in the aging population and a persistent clinical challenge. The increasing use of bioprosthetics as opposed to mechanical valves for aortic valve replacement has led to a rising number of cases requiring re-intervention for a failing bioprosthetic implant [1,2].

While surgical aortic valve replacement remains an established treatment for patients with acceptable operative risk, trans-catheter aortic valve implantation (TAVI) has emerged as a valuable alternative for patients with high operative risk [3-5] and is currently recommended for patients older than 75 years by the 2021 European Society of Cardiology/European Association for Cardiothoracic Surgery (ESC/EACTS) guidelines [6]. Redo cardiac surgery in patients with severe aortic stenosis and/or prosthetic valve dysfunction carries a mortality rate of 5-26% [7-9]; hence, a lower-risk, less-invasive percutaneous approach seems appealing. Nevertheless, patients with previous cardiac surgery have often been excluded from consideration of TAVI because of the risk of prosthetic displacement and coronary graft occlusion [7,10-12].

Several studies report the feasibility of valve-in-valve TAVI compared with redo aortic valve replacement (redo-AVR) for severe bioprosthetic aortic valve dysfunction, but mid- and long-term results are limited and patient cohorts are small [13-15].

This study sought to compare the outcomes of redo aortic valve replacement and valve-in-valve TAVI for patients with a failing bioprosthetic valve across the United Kingdom.

Materials and Methods

Study design and ethics statement

This report represents a retrospective observational study involving 11 centers. Patient data was retrospectively collected using standardized forms based on paper and electronic medical records. Institutional review board approval was granted in all participating centers.

The primary outcomes were in-hospital and mid-term mortality. Secondary outcomes included post-operative complications, rate of re-operation, length of intensive care unit stay (ICU), total in-hospital stay, and degree of post-intervention aortic valve regurgitation.

Hemodynamic outcomes, including post-procedural mean and peak gradients, were also assessed.

Patient involvement

This is a retrospective analysis; hence, direct patient involvement was not applicable. Nevertheless, patients are routinely informed of the anonymous use of their clinical data for research purposes in all participating centers.

Patient selection

All adult patients aged above 18 who had re-intervention (surgical AVR or valve-in-valve TAVI) for a failing surgical bioprosthesis were included. Patients were considered since the commencement of TAVI in each center; no patient having redo-AVR prior to that date was included. Patients in a critical pre-operative state, defined as pre-operative inotropic support, intravenous nitrates, ventilation, or cardiogenic shock, were included.

Exclusion criteria were: active endocarditis, previous cardiac surgery not including aortic valve replacement, concomitant coronary artery bypass grafting surgery, associated thoracic aortic surgery, or multiple valve intervention at the time of re-intervention. Patients who required a mechanical prosthesis at re-operation were excluded.

Propensity score analysis

Propensity score matching was used to adjust for confounding baseline differences between patients from different centers (Figure 1). A logistic regression model was used, with the intervention as the outcome variable and patients' characteristics as covariates. These included: age, hypertension, chronic kidney disease, Canadian Cardiovascular Society and New York Heart Association class, heart failure, pre-operative rhythm, pacemaker *in situ*, coronary artery disease, aortic valve pathology, pre-operative critical state, logistic EuroSCORE, national confidential inquiry into patient outcome and death priority, and the number and type of previous heart operations. The total sample was ranked by propensity score, and the resulting propensity-matched pairs were analyzed for differences in the outcomes of interest. The tolerance level applied was 0.01.

The matched valve-in-valve TAVI cohort mainly included patients treated after 2014 (85.6%, n=107), with only a few cases performed before that date (14.4%, n=18). This allowed us to tackle the change in practice/device for TAVI.

Data analysis

Continuous data are expressed as means ± standard deviation and analyzed with the analysis of variance test. Categorical data are expressed as percentages and counts and compared with the Pearson Chi-Square test.

Survival probabilities were estimated using Kaplan-Meier analysis; a log-rank test (Mantel-Cox) was used for comparison between groups. Follow-up time was calculated with the reverse Kaplan-Meier method. A multivariate-adjusted Cox regression analysis was also performed for mid-term mortality. Statistical significance was defined at $p<0.05$.

The SPSS system for statistics was used (released in 2019; SPSS Statistics for Windows, Version 26.0, IBM, Armonk, NY, USA). Propensity score matching was conducted independently by two authors (GG and YH) and checked by a different author (FG).

The statistical analysis was completed independently by four authors (FG, YH, GG, and PM).

Data availability statement

All relevant data are within the manuscript.

Results

Baseline characteristics

Between July 2005 and April 2021, 911 patients underwent redo-AVR and 411 valve-in-valve TAVI (Figure 2). After applying the exclusion criteria, there were 310 selected redo-AVR and 411 selected valve-in-valve TAVI. 125 pairs were included for analysis after propensity score matching. Demographics, clinical, and other pre-operative characteristics are summarized in Table 1. These were elderly patients with a mean age of 74.8±8.8 and 75.2±8.1 years for the matched surgical and interventional groups, p=0.7. Matched redo-AVR and valve-in-valve TAVI groups reported similar baseline characteristics.

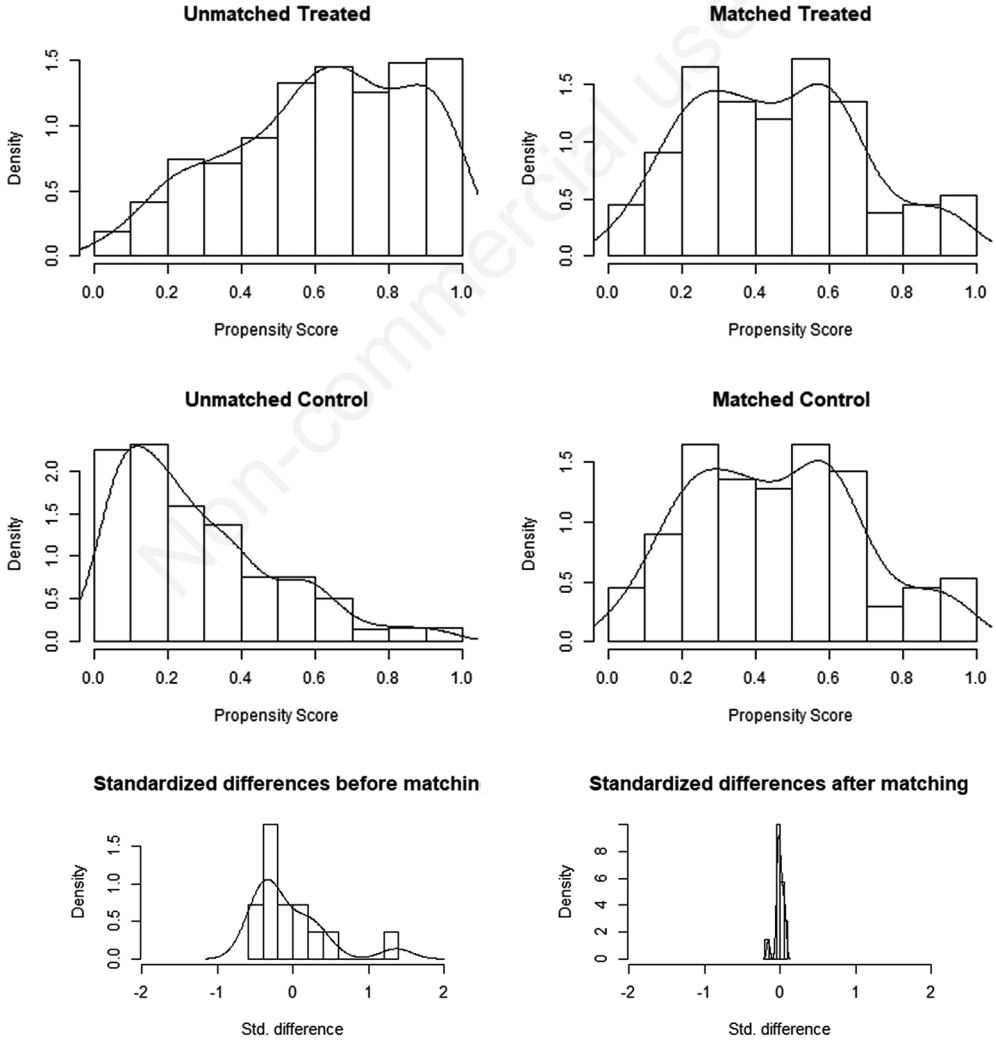

Figure 1. Propensity score distribution and standardized mean difference for unmatched and matched populations according to treatment groups.

Procedural characteristics

Procedural data for the redo-AVR and valve-in-valve TAVI cohorts are listed in Table 2. There was no requirement for conversion to surgery in the valve-in-valve TAVI group. The trans-catheter approaches adopted were femoral (95.2%, n=119), subclavian (4%, n=5), and trans-apical (0.8%, n=1).

Valve size and type for both explanted and implanted prostheses are reported in Table 3. Patients undergoing valve-in-valve TAVI received a larger valve prosthesis (p<0.001). A wide range of implants was used in the two groups (p<0.001).

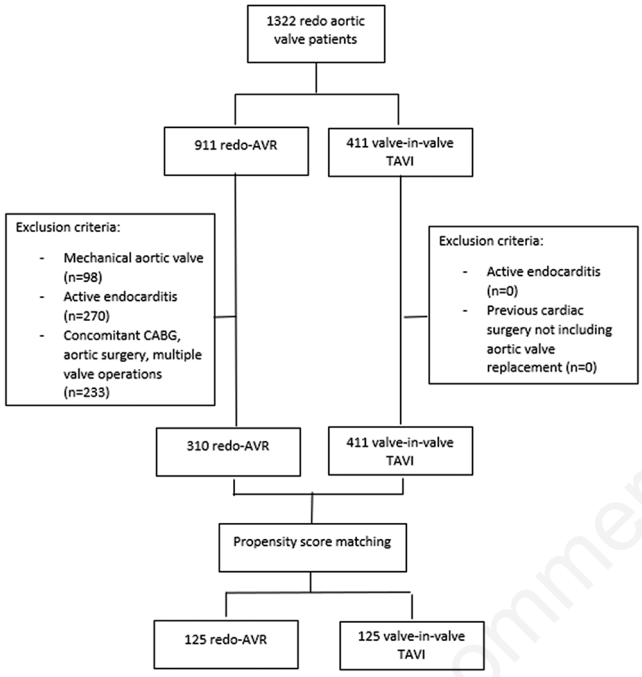

Figure 2. Patient selection. AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation; CABG, coronary artery bypass graft.

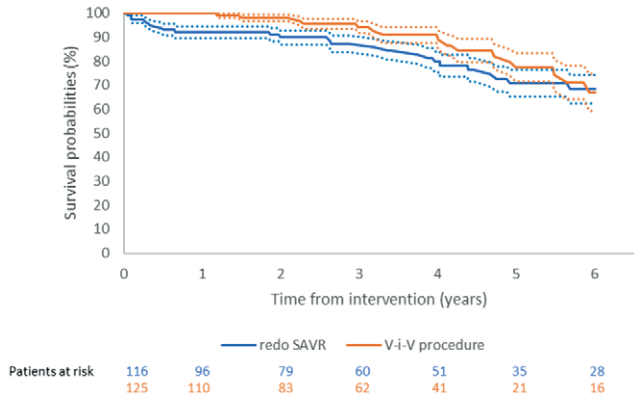

Figure 3. Kaplan-Meier curves of survival probabilities for propensity-matched redo aortic valve replacement and valve-in-valve trans-catheter aortic valve implantation populations. SAVR, surgical aortic valve replacement; V-i-V, valve-in-valve.

Primary outcomes

The comparative analysis of in-hospital and mid-term mortality in patients undergoing redo-AVR and valve-in-valve TAVI resulted in statistically significant results (Table 4). In-hospital mortality was 7.2% (n=9) for the former and 0 for the latter (p=0.002).

The median follow-up was 4.2 (2.0; 7.2) years for redo-AVR, and 3.1 (1.8; 5.8) years for valve-in-valve TAVI (p=0.09). Among patients who were successfully discharged from the hospital, survival probabilities after redo-AVR were: 92±2.5% at 1 year, 90±2.9% at 2-year, 87±3.4% at 3-year, 80±4.5% at 4-year, 70±5.5% at 5-year, and 68±5.8% at 6-year follow-up. Survival probabilities after valve-in-valve TAVI were: 100% at 1-year, 98±1.3% at 2-year, 94±2.5% at 3-year, 89±3.9% at 4-year, 77±5.9% at 5-year, and 67±7.6% at 6-year follow-up. Log-rank test had p=0.26 (Figure 3).

Cox regression analysis

A multivariate-adjusted Cox regression analysis of factors impacting mid-term mortality was performed, including age, sex, logistic EuroSCORE, explant valve size, and year of intervention (Table 5).

Based on the multivariate model, there was no difference in survival in relation to age [hazard ratio (HR) 1.02, confidence interval (CI) (0.98;1.05), p=0.3], sex [HR 1.18, CI (0.66;2.10), p=0.6], logistic EuroSCORE [HR 1.02, CI (0.99;1.04), p=0.1], and explant valve size [HR 1.02, CI (0.88;1.19), p=0.8] for the matched populations. Mid-term survival was not different for year of intervention [<2015 *versus* >2018 HR 1.81, CI (0.72;4.55) p=0.2 and 2015-2018 *versus* >2018 HR 1.67, CI (0.66;4.25) p=0.3].

Secondary outcomes

Post-procedural clinical outcomes in redo-AVR and valve-in-valve TAVI are reported in Table 4. Surgical intervention accounted for greater intra-aortic balloon pump support, re-operation for bleeding, post-operative complications, and prolonged hospitalization. Respiratory complications included prolonged mechanical ventilation, pulmonary edema, pneumothorax and pleural effusion requiring chest drain insertion, and nosocomial pneumonia. Neurological complications refer to transient ischaemic attack and stroke.

At discharge, patients undergoing valve-in-valve TAVI reported significantly higher grades of aortic regurgitation. A large proportion of patients undergoing the percutaneous approach had moderate aortic regurgitation (p<0.001), compared with 92% of surgical patients having none (Table 6). Pre-procedural and post-procedural gradients for both approaches are reported in Table 6; valve-in-valve TAVI was associated with higher mean and peak gradients at discharge (p<0.001).

Discussion

This multicenter study reports early and mid-term outcomes for aortic valve re-intervention for bioprosthetic aortic valve dysfunction across the United Kingdom. In the elderly population studied, valve-in-valve TAVI carries a more favorable morbidity and early mortality profile than redo aortic valve replacement. The 2021 ESC/EACTS guidelines for the management of valvular heart disease suggest TAVI as the primary intervention for severe native aortic valve stenosis in patients older than 75 years [6]. However, the choice between valve-in-valve TAVI and redo-AVR in patients with aortic prosthetic dysfunction lacks evidence and

Table 1. Baseline characteristics of non-propensity-matched and propensity-matched patients in redo aortic valve replacement and valve-in-valve trans-catheter aortic valve implantation.

	Non-matched Redo-AVR (n=310)	Valve-in-valve TAVI (n=411)	p	Redo-AVR (n=125)	Valve-in-valve TAVI (n=125)	p
Age, years±SD	71.3±12.7	77.9±7.5	<0.001	74.8±8.8	75.2±8.1	0.7
Male, % (n)	64.2 (199)	57.7 (237)	0.08	63.2 (79)	58.4 (73)	0.4
BMI, kg/m^2±SD	27.7±4.9	27.4±5.1	0.5	27.5±4.6	27.5±5.4	0.9
Hypertension, % (n)	63.9 (198)	79.6 (327)	<0.001	75.2 (94)	78.4 (98)	0.5
Diabetes mellitus, % (n)	18.7 (58)	20.4 (84)	0.5	20.8 (26)	24.0 (30)	0.5
COPD, % (n)	19.0 (59)	20.9 (86)	0.5	18.4 (23)	22.4 (28)	0.4
Chronic kidney disease, % (n)	5.2 (16)	13.4 (55)	<0.001	7.2 (9)	9.6 (12)	0.5
Previous TIA/stroke, % (n)	11.6 (36)	12.2 (50)	0.8	9.6 (12)	12.8 (16)	0.4
CCS class, % (n)			0.002			0.6
Class I	73.2 (227)	83.5 (343)		81.6 (102)	(96)	
Class II	17.1 (53)	9.0 (37)		12.0 (15)	(18)	
Class III	8.7 (27)	5.6 (23)		6.4 (8)	8.0 (10)	
Class IV	1.0 (3)	1.9 (8)		0	0.8 (1)	
NYHA class, % (n)			<0.001			0.5
Class I	8.7 (27)	3.4 (14)		8.8 (11)	(6)	
Class II	26.1 (81)	14.6 (60)		17.6 (22)	(28)	
Class III	50.3 (156)	60.1 (247)		57.6 (72)	55.2 (69)	
Class IV	14.8 (46)	21.9 (90)		16 (20)	17.6 (22)	
Ejection fraction, % (n)			0.05			0.8
Good (>49)	70.0 (217)	61.8 (254)		70.4 (88)	(91)	
Fair (30-49)	23.5 (73)	28.0 (115)		23.2 (29)	22.4 (28)	
Poor (<30)	6.5 (20)	10.2 (42)		6.4 (8)	4.8 (6)	
Previous myocardial infarction, % (n)	16.8 (52)	21.9 (90)	0.09	17.6 (22)	14.4 (18)	0.5
Heart failure, % (n)	12.6 (39)	24.3 (100)	<0.001	16.0 (20)	15.2 (19)	0.9
Rhythm, % (n)			<0.001			0.3
Sinus	83.5 (259)	60.6 (249)		73.6 (92)	64.0 (80)	
Atrial fibrillation/atrial flutter	12.6 (39)	32.4 (133)		21.6 (27)	29.6 (37)	
Complete heart block	3.9 (12)	7.1 (29)		4.8 (6)	6.4 (8)	
Pacemaker	3.5 (11)	8.0 (33)	0.01	5.6 (7)	6.4 (8)	0.8
Coronary artery disease, % (n)			<0.001			0.2
Not investigated	5.5 (17)	10.7 (44)		8.8 (11)	2.4 (3)	
None	81.0 (251)	67.9 (279)		75.2 (94)	(107)	
Single-vessel	10.0 (31)	12.2 (50)		12.0 (15)	(12)	
Two-vessel	2.3 (7)	8.0 (33)		2.4 (3)	1.6 (2)	
Three-vessels	1.3 (4)	1.2 (5)		1.6 (2)	0.8 (1)	
Aortic valve pathology, % (n)			0.03			0.7
Stenosis	28.7% (89)	35.5 (146)		31.2 (39)	(33)	
Regurgitation	45.8 (142)	36.0 (148)		39.2 (49)	41.6 (52)	
Mixed	25.5 (79)	28.5 (117)		29.6 (37)	32.0 (40)	
Logistic EuroSCORE, %±SD	20.6±13.2	14.9±9.0	<0.001	17.8±9.1	17.9±11.3	0.9
NCEPOD priority, % (n)			0.005			0.6
Elective	54.5 (169)	65.9 (271)		64 (80)	(72)	
Urgent	40 (124)	31.1 (128)		32.8 (41)	(49)	
Emergency	5.5 (17)	2.9 (12)		3.2 (4)	3.2 (4)	
Pre-operative critical state, % (n)	9.7 (30)	4.6 (19)	0.008	4.8 (6)	7.2 (9)	0.4
Previous cardiac surgery, % (n)			0.001			0.6
One procedure	92.3 (288)	86.1 (354)		92.8 (116)	(118)	
Two procedures	6.5 (20)	13.6 (56)		7.2 (9)	(7)	
Three procedures	1.3 (4)	-		-	-	
Four procedures	-	0.2 (1)		-	-	
Type of previous cardiac surgery, % (n)			<0.001			0.5
Isolated AVR	93.2 (289)	71.3 (293)		90.4 (113)	(110)	
AVR and CABG	3.2 (10)	25.5 (105)		6.4 (8)	(7)	
AVR and aortic Surgery	1.9 (6)	1.7 (7)		1.6 (2)	1.6 (2)	
AVR and congenital	1.6 (85)	1.5 (6)		1.6 (2)	4.8 (6)	

AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation; SD, standard deviation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association; NCEPOD, national confidential inquiry into patient outcome and death; TIA, transient ischaemic attack; CABG, coronary artery bypass graft.

relies on the individual patient's assessment. Our analysis adds mid-term survival data to support decision-making in the population studied.

The analysis of mortality revealed significant differences between the two treatment options. Redo-AVR led to higher in-hospital mortality compared with valve-in-valve TAVI. Our results align with recent evidence. Deharo *et al.* showed a significant difference in the outcomes of valve-in-valve TAVI by time period, with better results after 2015 [16]. In our analysis, mid-term mortality did not differ in relation to age, sex, logistic EuroSCORE, explant valve size, or year of intervention. It is important to note that 92% of our matched TAVI cases were performed after 2014. The same study reported that valve-in-valve TAVI was associated with lower 30-day mortality than redo surgical AVR (p=0.02) [16]. Another recent Canadian study demonstrated lower 30-day mortality (95% CI: -12.6% to -2.3%) and increased 5-year survival (p=0.04) for trans-catheter aortic valve replacement [17]; our study corroborates such findings in Europe. Patel *et al.* showed similar figures in early mortality for the two interventions (p=0.92), in a non-matched analysis, where the trans-catheter group was older than the surgical one (p=0.01) [18]. Earlier studies reflecting the activity before 2015 reported different results; 30-day mortality was similar for redo-AVR and valve-in-valve TAVI [13,15,19], with one-year survival favoring surgery in a single center [13]. However, these are mainly single-center, unmatched studies, and the redo-TAVI cohort included all patients with previous cardiac

Table 2. Procedural characteristics of the propensity-matched patients in redo aortic valve replacement and valve-in-valve trans-catheter aortic valve implantation.

	Redo-AVR (n=125)	Valve-in-valve TAVI (n=125)	p
Year of intervention, % (n)			<0.001
<2015	40 (50)	(18)	
2015-2018	30.4 (38)	51.2 (64)	
>2018	29.6 (37)	34.4 (43)	
Previous valvuloplasty, % (n)	-	2.4 (3)	0.08
TAVI approach, % (n)			
Femoral	-	(119)	
Subclavian	-	4.0 (5)	
Trans-apical	-	0.8 (1)	
Pre-procedural valvuloplasty, % (n)	-	10.4 (13)	
Post-procedural valvuloplasty, % (n)	-	12.8 (16)	
Neuroprotection, % (n)	-	5.6 (7)	0.007
CPB duration, min±SD	142.2±62.4	-	
Ischaemic time min±SD	91.3±36.3	-	

AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation; SD, standard deviation; CPB, cardiopulmonary bypass.

Table 3. Valve size and type of the propensity-matched patients in redo aortic valve replacement and valve-in-valve trans-catheter aortic valve implantation.

	Explant Redo-AVR	Valve-in-valve TAVI	p	Implant Redo-AVR	Valve-in-valve TAVI	p
Valve size, % (n)			0.003			<0.001
≤23	77.6 (97)	60 (75)		76 (95)	19.2 (24)	
>23	22.4 (28)	40 (50)		24 (30)	80.8 (101)	
Valve type, % (n)			0.1			<0.001
Boston Accurate	-	-		-	(6)	
Edwards Perimount	14.4 (18)	19.2 (24)		(52)	-	
Edwards Sapien 3	-	-		-	(21)	
Edwards Intuity	-	-		(2)	-	
Elan Stentless	4 (5)	2.4 (3)		(1)	-	
Epic	7.2 (9)	5.6 (7)		(16)	-	
Epic Supra	-	-		(5)	-	
Evolut	-	-		-	(28)	
Freestyle	0.8 (1)	1.6 (2)		(3)	-	
Hancock	2.4 (3)	0.8 (1)		(9)	-	
Lotus	-	-		-	(3)	
Mitroflow	10.4 (13)	9.6 (12)		(2)	-	
Mosaic	3.2 (4)	4.8 (6)		-	-	
Portico	-	-		-	(3)	
Sorin	4.8 (6)	-		1.6 (2)	-	
Trifecta	4.8 (6)	9.6 (12)		15.2 (19)	-	
Other	7.2 (9)	1.6 (2)		4.8 (6)	4 (5)	

AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation.

surgery, irrespective of previous surgical AVR. Such a difference might impact outcomes, as shown in other redo situations [7].

In our study, early clinical outcomes are significantly in favor of the valve-in-valve TAVI approach. Surgical patients required a prolonged ICU and hospital stay. Similar results were reported by Giordano *et al.* (p<0.001) and Wilbring *et al.* (p=0.0216) [14,19]. Several studies have also confirmed greater complication rates for redo-AVR in comparison with valve-in-valve TAVI, including a higher rate of stroke, myocardial infarction, major bleeding complications, and PPM implantation [13,15,16,20].

Post-procedural aortic regurgitation remains a significant concern after TAVI, even for valve-in-valve procedures in degenerated bioprosthetic valves. Our study demonstrated a higher incidence of post-procedural aortic regurgitation (AR) in patients undergoing

Table 4. The post-procedural clinical course of the non-propensity-matched and propensity-matched patients in redo aortic valve replacement and valve-in-valve trans-catheter aortic valve implantation.

	Non-matched Redo-AVR (n=310)	Valve-in-valve TAVI (n=411)	p	Redo-AVR (n=125)	Valve-in-valve TAVI (n=125)	p
IABP, % (n)	2.3 (7)	-	0.002	4.0 (5)	-	0.02
Vascular access complications, % (n)	-	8.8 (36)		-	9.6 (12)	
Re-operation for bleeding, % (n)	19.7 (61)	1.2 (5)	<0.001	22.4 (28)	2.4 (3)	<0.001
Myocardial infarction, % (n)	1.3 (4)	1.2 (5)	0.9	0.8 (1)	1.6 (2)	0.6
Arrhythmias, % (n)	21.3 (66)	2.2 (9)	<0.001	26.4 (33)	0.8 (1)	<0.001
PPM implantation, % (n)	8.7 (27)	2.9 (12)	<0.001	8.8 (11)	3.2 (4)	0.06
Respiratory complications, % (n)	14.5 (45)	6.6 (27)	<0.001	17.6 (22)	8.0 (10)	0.02
Acute kidney injury, % (n)	7.7 (24)	4.4 (18)	0.06	8.0 (10)	4.8 (6)	0.3
Neurological complications, % (n)	5.5 (17)	1.7 (7)	0.005	7.2 (9)	1.6 (2)	0.03
Wound complications, % (n)	2.3 (7)	1.9 (8)	0.8	1.6 (2)	2.4 (3)	0.6
MOF, % (n)	3.9 (12)	0.5 (2)	0.001	4.8 (6)	-	0.01
ICU stay hours±SD	122.7±145.8	48.7±165.9	<0.001	126.7±181.3	45.2±107.8	<0.001
Hospital stay days±SD	14.2±12.9	8.5±13.5	<0.001	14.1±13.5	8.6±11.4	<0.001
In-hospital mortality, % (n)	4.8 (15)	1.2 (5)	0.003	7.2 (9)	-	0.002

AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation; IABP, intra-aortic balloon pump; PPM, permanent pacemaker; MOF, multiple organ failure; ICU, intensive care unit; SD, standard deviation.

Table 5. Multivariant adjusted Cox regression analysis for mid-term mortality.

	HR	(95% CI)	p
Age	1.02	(0.98; 1.05)	0.3
Sex	1.18	(0.66; 2.10)	0.6
Logistic EuroSCORE	1.02	(0.99; 1.04)	0.1
Explant valve size	1.02	(0.88; 1.19)	0.8
Year of intervention			
<2015 *versus* >2018	1.81	(0.72; 4.55)	0.2
2015-2018 *versus* >2018	1.67	(0.66; 4.25)	0.3

HR, hazard ratio; CI, confidence interval.

Table 6. Aortic regurgitation at discharge, pre- and post-procedural gradients of propensity-matched populations.

	Redo-AVR (n=125)	Valve-in-valve TAVI (n=125)	p
No AR, % (n)	92.0 (115)	78.4 (98)	0.002
Mild AR, % (n)	6.4 (8)	6.4 (8)	1
Moderate AR, % (n)	1.6 (2)	15.2 (19)	<0.001
Severe AR, % (n)	-	-	
Pre-procedure mean gradient, mmHg±SD	34.7±20.4	39.5±22.0	0.1
Pre-procedure peak gradient, mmHg±SD	63.4±33.1	65.7±34.1	0.6
Post-procedure mean gradient, mmHg±SD	11.9±4.6	17.6±9.7	<0.001
Post-procedure peak gradient, mmHg±SD	23.0±8.1	31.6±18.1	<0.001

AR, aortic regurgitation; AVR, aortic valve replacement; TAVI, trans-catheter aortic valve implantation; SD, standard deviation.

valve-in-valve TAVI instead of redo-AVR. In the PARTNER trial, moderate to severe AR was observed in 6.8% of patients undergoing TAVI, compared to 1.9% for surgical AVR at one-year follow-up [4]. In the UK TAVI registry, 61% of patients had some degree of AR, with greater than moderate severity in 13.5% [20]. In the global valve-in-valve registry, 5% of patients had ≥+2 degrees of AR after the procedure [21]. Similarly, in a recent study, 3.7% of patients treated with the same intervention reported moderate AR at one year [22]. Finally, a study from Cleveland showed the presence of moderate-severe aortic regurgitation in 30.4% of patients undergoing valve-in-valve TAVI [23].

Valve-in-valve TAVI may lead to patient-prosthesis mismatch with higher mean and peak gradients at 1-year follow-up compared with native valve TAVI and redo-AVR [24-28]. Similarly, our study reported higher mean and peak gradients at discharge for patients treated with the percutaneous intervention.

The occurrence of significant AR and higher post-procedural gradients, which we report in line with the literature, would be expected to impact the development of heart failure, resulting in a worse quality of life and survival rate. Such factors may be acceptable in the elderly category of patients our analysis includes, particularly given the more favorable morbidity and early mortality. However, these may be relevant to younger patients with a longer life expectancy who require lifetime management. Furthermore, in elderly patients where valve-in-valve TAVI would result in a smaller bioprosthetic size or a higher risk of coronary occlusion, redo-AVR would still be a valid alternative with a similar mid-term survival.

Limitations

Echocardiographic data, including mean and peak gradients, was missing in less than 10% of the matched populations. Similarly, echocardiographic data on the feasibility criteria for valve-in-valve TAVI, such as the degree of left ventricle hypertrophy and outflow tract obstruction, the aortic root size, and the extent of calcification, was not reported. However, in each center included in our study, patients were discussed at multidisciplinary meetings, and the decision for either intervention was made accordingly.

The multicenter design allowed for the collection of over 700 selected cases requiring re-intervention for a failing surgical bioprosthesis, but the baseline differences between groups led to a much smaller cohort of matched pairs for analysis after propensity score matching. Nevertheless, a randomized controlled trial would be advisable to tackle the baseline differences between the two categories of patients.

Mid-term mortality according to valve type was not analyzed because of the diversity of prostheses and the small number at risk.

Finally, different recruitment periods at various centers, reflecting the introduction of TAVI, the activity of each hospital, and the different levels of expertise of performing clinicians, might have an impact on the outcomes.

Conclusions

In elderly patients with a degenerated bioprosthetic valve, valve-in-valve TAVI, as opposed to redo-AVR with a biological prosthesis, carries better morbidity and early survival. The degree of aortic regurgitation and higher post-procedural gradients must be acknowledged when valve-in-valve TAVI is performed in a younger age cohort.

References

1. Onorati F, Biancari F, De Feo M, et al. Mid-term results of aortic valve surgery in redo scenarios in the current practice: results from the multicentre European RECORD (REdo Cardiac operation research database) initiative. Eur J Cardiothorac Surg 2015;47:269-80.
2. Maganti M, Rao V, Armstrong S, et al. Redo valvular surgery in elderly patients. Ann Thorac Surg 2009;87:521-5.
3. Stachon P, Kaier K, Zirlik A, et al. Risk-adjusted comparison of in-hospital outcomes of transcatheter and surgical aortic valve replacement. J Am Heart Assoc 2019;8:e011504.
4. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic valve replacement in high-risk patients. N Engl J Med 2011;364:2187-98.
5. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012;366:1686-95.
6. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Rev Esp Cardiol 2022;75:524.
7. Jones JM, O'kane H, Gladstone DJ, et al. Repeat heart valve surgery - risk factors for operative mortality?. J Thorac Cardiovasc Surg 2001;122:913-8.
8. Akins CW, Buckley MJ, Daggett WM, et al. Risk of preoperative valve replacement for failed mitral and aortic bioprostheses. Ann Thorac Surg 1998;65:1545-52.
9. Jamieson WRE, Burr LH, Miyagishima RT, et al. Reoperation for bioprosthetic aortic structural failure - risk assessment. Eur J Cardiothorac Surg 2003;24:873-8.
10. Chmielak Z, Dabrowski M, Tyczynski P, et al. Transcatheter aortic valve replacement in patients with previous mitral valve replacement. A systematic study. Postepy Kardiol Interwencyjnej 2020;16:177-83.
11. Bruschi G, De Marco F, Barosi A, et al. Self-expandable transcatheter aortic valve implantation for aortic stenosis after mitral valve surgery. Interact Cardiovasc Thorac Surg 2013; 17:90-5.
12. Hulman M, Bena M, Artemious P, et al. Transaortic approach for transcatheter aortic valve replacement with other concomitant cardiac procedures in high-risk patients. J Card Surg 2016;31:493-7.
13. Erlebach M, Wottke M, Deutsch MA, et al. Redo aortic valve surgery versus transcatheter valve-in-valve implantation for failing surgical bioprosthetic valves: consecutive patients in a single-center setting. J Thorac Dis 2015;7:1494-500.
14. Giordano V, Kar A, Flapan A, et al. Alternative treatment option for high risk surgical candidates after previous cardiac surgery: the Scottish national TAVI programme experience. J Cardiothorac Surg 2015;10:A236.
15. Papadopoulos N, Schiller N, Fichtlscherer S, et al. Propensity matched analysis of longterm outcomes following transcatheter based aortic valve implantation versus classic aortic valve replacement in patients with previous cardiac surgery. J Cardiothorac Surg 2014;9:99.
16. Deharo P, Bisson A, Herbert J, et al. Transcatheter valve-in-valve aortic valve replacement as an alternative to surgical re-replacement. J Am Coll Cardiol 2020;76:489-99.
17. Tam DY, Dharma C, Rocha RV, et al Transcatheter ViV versus

redo surgical AVR for the management of failed biological prosthesis: early and late outcomes in a propensity-matched cohort. JACC Cardiovasc Interv 2020;13:765-74.
18. Patel PM, Chious E, Cao Y, et al. Isolated redo-aortic valve replacement versus valve-in-valve transcatheter valve replacement. Ann Thorac Surg 2021;112:539-45.
19. Wilbring M, Tugtekin SM, Alexious K, et al. Transapical transcatheter aortic valve implantation vs conventional aortic valve replacement in high-risk patients with previous cardiac surgery: a propensity-score analysis. Eur J Cardiothorac Surg 2013;44:42-7.
20. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the UK TAVI (United Kingdom transcatheter aortic valve implantation) registry. J Am Coll Cardiol 2011;58:2130-8.
21. Dvir D, Webb J, Brecker S, et al. Transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: results from the global valve-in-valve registry. Circulation 2012;126:2335-44.
22. Pravda NS, Kornowski R, Levi A, et al. 5 year outcomes of patients with aortic structural valve deterioration treated with transcatheter valve in valve - a single centre prospective registry. Front Cardiovasc Med 2021;9:713341.
23. Abushouk AIA, Abdelfattah O, Saad A, et al. Predictors of procedural success in patients with degenerated surgical valves undergoing transcatheter aortic valve-in-valve implantation. Front Cardiovasc Med 2021;24:718835.
24. Akodad M, Meilhac A, Lefevre T, et al. Hemodynamic performances and clinical outcomes in patients undergoing valve-in-valve versus native transcatheter aortic valve implantation. Am J Cardiol 2019;124:90-7.
25. Tang GHL, Sengupta A, Alexis SL, et al. Outcomes of prosthesis-patient mismatch following supra-annular transcatheter aortic valve replacement: from the STS/ACC TVT Registry. JACC Cardiovasc Interv 2021;14:964-76.
26. Sedeek AF, Greason KL, Sandhu GS, et al. Transcatheter valve-in-valve vs surgical replacement of failing stented aortic biological valves. Ann Thorac Surg 2019;108:424-30.
27. Balsam LB, Grossi EA, Greenhouse DG, et al. Reoperative valve surgery in the elderly: predictors of risk and longterm survival. Ann Thorac Surg 2010;90:1195-200.
28. Gotzmann M, Lindstaedt M, Mugge A. From pressure overload to volume overload: aortic regurgitation after transcatheter aortic valve implantation. Am Heart J 2012;163:903-11.