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NEW RESEARCH PAPER

STRUCTURAL

Explant vs Redo-TAVR After Transcatheter Valve Failure

Mid-Term Outcomes From the EXPLANTORREDO-TAVR International Registry

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ABBREVIATIONS AND ACRONYMS

AV = aortic valve

BEV = balloon-expandable valve

CKD = chronic kidney disease

PPM = prosthesis-patient mismatch

PVL = paravalvular leak

SAVR = surgical aortic valve replacement

STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality

SVD = structural valve degeneration

TAVR = transcatheter aortic valve replacement

TAVR-explant = transcatheter aortic valve replacement surgical explantation

THV = transcatheter heart valve

ABSTRACT

BACKGROUND Valve reintervention after transcatheter aortic valve replacement (TAVR) failure has not been studied in detail.

OBJECTIVES The authors sought to determine outcomes of TAVR surgical explantation (TAVR-explant) vs redo-TAVR because they are largely unknown.

METHODS From May 2009 to February 2022, 396 patients in the international EXPLANTORREDO-TAVR registry underwent TAVR-explant (181, 46.4%) or redo-TAVR (215, 54.3%) for transcatheter heart valve (THV) failure during a separate admission from the initial TAVR. Outcomes were reported at 30 days and 1 year.

RESULTS The incidence of reintervention after THV failure was 0.59% with increasing volume during the study period. Median time from index-TAVR to reintervention was shorter in TAVR-explant vs redo-TAVR (17.6 months [IQR: 5.0-40.7 months] vs 45.7 months [IQR: 10.6-75.6 months]; $P < 0.001$], respectively. TAVR-explant had more prosthesis-patient mismatch (17.1% vs 0.5%; $P < 0.001$) as the indication for reintervention, whereas redo-TAVR had more structural valve degeneration (63.7% vs 51.9%; $P = 0.023$), with a similar incidence of ≥moderate paravalvular leak between groups (28.7% vs 32.8% in redo-TAVR; $P = 0.44$). There was a similar proportion of balloon-expandable THV failures (39.8% TAVR-explant vs 40.5% redo-TAVR; $P = 0.92$). Median follow-up was 11.3 (IQR: 1.6-27.1 months) after reintervention. Compared with redo-TAVR, TAVR-explant had higher mortality at 30 days (13.6% vs 3.4%; $P < 0.001$) and 1 year (32.4% vs 15.4%; $P = 0.001$), with similar stroke rates between groups. On landmark analysis, mortality was similar between groups after 30 days ($P = 0.91$).

CONCLUSIONS In this first report of the EXPLANTORREDO-TAVR global registry, TAVR-explant had a shorter median time to reintervention, with less structural valve degeneration, more prosthesis-patient mismatch, and similar paravalvular leak rates compared with redo-TAVR. TAVR-explant had higher mortality at 30 days and 1 year, but similar rates on landmark analysis after 30 days. (J Am Coll Cardiol Intv 2023;16:927–941)
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Transcatheter aortic valve (AV) replacement (TAVR) is now approved across all surgical risk profiles. As TAVR expands to younger, lower-risk patients with longer life expectancies, reintervention is likely to become more common. Given that long-term data on transcatheter heart valve (THV) durability are limited, lifetime management of aortic stenosis and THV failure is becoming more important. There are currently 2 treatment strategies for THV failure: redo-TAVR or surgical explantation of TAVR (TAVR-explant),[1-3] with redo-TAVR having more favorable 30-day outcomes compared with TAVR-explant,[4,5] We have previously reported mid-term outcomes of TAVR-explant in the international EXPLANT-TAVR registry.[1] Other registry studies have also reported the incidence, characteristics, and outcomes from each group independently,[3,6,7] but none have compared the 2 groups across the same centers and included detailed procedural and imaging data. It also remains unclear which treatment option is preferred, as each may have certain inherent limitations. For example, redo-TAVR (TAV-in-TAV) may not be feasible in a subgroup of patients who have unfavorable anatomy or may not be appropriate due to a prior valve-in-valve procedure.[1,8] We therefore sought to evaluate the incidence, characteristics, and outcomes of patients who had TAVR-explant or redo-TAVR, specifically in patients with THV failure, that were not acute or due to endocarditis, in a multicenter international registry.

METHODS

DATA SOURCE. The EXPLANTORREDO-TAVR registry is a multicenter, international registry of patients who underwent TAVR-explant or redo-TAVR for THV failure. This registry included 29 centers performing both surgical and transcatheter reintervention for THV failure, between May 2009 and February 2022. Initial TAVR was performed between June 2007 and November 2021, and was not limited to only our participating centers, given a proportion of patients

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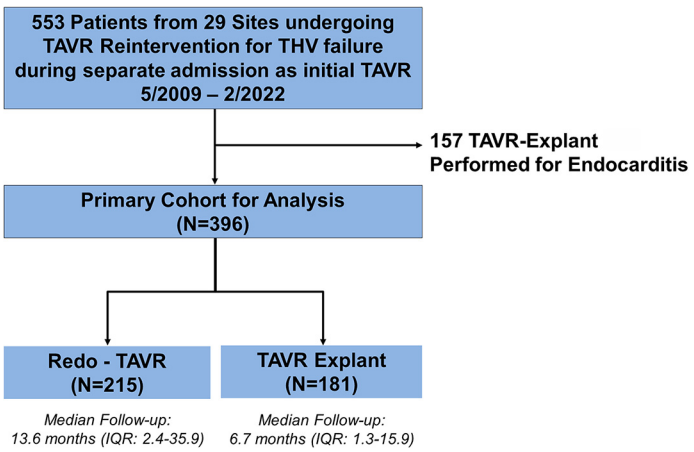
who underwent reintervention at our centers had TAVR at outside institutions (Supplemental Figure S1). Anonymized data were obtained from each institution's electronic health records with detailed information on clinical characteristics, echocardiographic profiles, mechanisms of THV failure, timing and indications for reintervention, in addition to outcomes at 30 days, 1 year, and beyond. Because all participating institutions contributed cases after obtaining local institutional review board approvals, the requirement to obtain patient consent was waived. The 30-day and longer-term follow-up of all subjects in this registry were adjudicated separately by each individual institution.

PATIENT POPULATION. All adult patients who underwent TAVR-explant or redo-TAVR for THV failure due to, but not limited to, the following conditions were included: structural valve degeneration (SVD), ≥moderate paravalvular leak (PVL), severe prosthesis-patient mismatch (PPM), THV thrombosis, or delayed prosthetic valve migration as defined by Valve Academic Research Consortium-3 criteria.[9] Our study cohort (N = 396) was stratified into patients undergoing redo-TAVR (n = 215, 54.3%) and TAVR-explant (n = 181, 45.7%) for THV failure (Figure 1). Because our study focus was to compare reinterventions for THV failure, redo-TAVR performed during the same admission as the initial TAVR (ie, all "bailout" TAVR) were excluded. Similarly, patients who required emergency surgical conversion immediately after TAVR or surgical intervention within the same hospitalization were excluded from the study. TAVR-explant performed for endocarditis was also excluded.

The decision to perform TAVR-explant or redo-TAVR was determined by the multidisciplinary heart teams at their respective institutions. The volume of index-TAVR procedures performed outside participating centers referred to participating sites and number of qualifying patients who did not undergo or were declined reintervention were not captured in our study.

OUTCOMES OF INTEREST AND DEFINITIONS. We sought to determine outcomes of TAVR-explant vs redo-TAVR for THV failure. The primary outcomes of interest included cumulative mortality, and the in-hospital, 30-day, and 1-year mortality after reintervention. Our secondary outcomes of interest were median interval from index-TAVR procedure to reintervention, median hospital length of stay, in-hospital complication rates (eg, stroke, vascular complication, new pacemaker, life-threatening/major bleed), and 30-day stroke rates. All clinical endpoints, including the severity of PVL and transvalvular aortic regurgitation, were reported according to the Valve Academic Research Consortium-3 criteria.[9]

FIGURE 1 Study Population



From May 2009 to February 2022, 553 patients from 29 sites in the international EXPLANTORREDO-TAVR registry underwent transcatheter aortic valve replacement (TAVR) explantation (TAVR-explant) or redo-TAVR for transcatheter valve failure during a separate admission as the initial TAVR. All TAVR-explants performed for endocarditis (n = 157, 46.4%) were excluded. Incidence, characteristics, and mid-term outcomes of 215 redo-TAVR (54.3%) were compared with 181 TAVR-explant (45.7%) across the same centers. THV = transcatheter heart valve.

Timing of reintervention was classified as emergency, urgent, or elective based on the interval between initial decision to perform reintervention and TAVR-explant or redo-TAVR: <6 hours of the initial diagnosis of THV failure was considered emergency; in the same hospital admission as the initial diagnosis was considered urgent; on a separate hospital admission as the initial diagnosis was considered elective.

The median interval from index-TAVR to reintervention was calculated in months from the date of the initial TAVR procedure to the date of reintervention. Survival time was counted in months from the date of reintervention to mortality date or date of last follow-up if the patients were recorded as alive. Follow-up for the study cohort was 96.7% complete at 30 days following reintervention and 80.3% complete at 1 year among patients eligible for follow-up at these intervals.

STATISTICAL ANALYSES. Baseline demographic, clinical characteristics, and echocardiographic parameters were collected for all patients at the time of index-TAVR procedure and subsequent

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TABLE 1 Patient Characteristics at the Time of Index TAVR

	Overall (N = 396)	Redo-TAVR (n = 215)	TAVR-Explant (n = 181)	*P* Value
Age, y	75.5 ± 9.3	78.6 ± 8.4	72.1 ± 9	<0.001
Female	162 (40.9)	95 (44.2)	67 (37)	0.15
Frailty	106 (34.3)	53 (36.3)	53 (32.5)	0.55
Coronary artery disease	214 (56.5)	106 (52.2)	108 (61.4)	0.078
Stroke	53 (13.9)	31 (15.3)	22 (12.4)	0.46
Cerebrovascular disease	72 (22.4)	34 (23.4)	38 (21.5)	0.69
Peripheral vascular disease	81 (21.3)	48 (23.6)	33 (18.6)	0.26
Diabetes	111 (29.1)	54 (26.6)	57 (32)	0.26
Atrial fibrillation	149 (39.1)	74 (36.5)	75 (42.1)	0.29
Pulmonary hypertension	95 (25.5)	47 (23.2)	48 (28.2)	0.28
Chronic kidney disease	152 (40.6)	76 (37.4)	76 (44.4)	0.17
Dialysis-dependent	29 (7.6)	16 (7.9)	13 (7.3)	1.00
Chronic obstructive pulmonary disease	94 (24.7)	48 (23.6)	46 (26)	0.63
Hostile chest or chest deformity	45 (13)	24 (14)	21 (12.1)	0.63
Calcified aorta	61 (16.2)	50 (24.5)	11 (6.4)	<0.001
Left ventricular ejection fraction, %	51.8 ± 13	52.7 ± 12.4	50.9 ± 13.6	0.21
Prior permanent pacemaker/ICD	82 (21.5)	41 (20.2)	41 (23)	0.53
Prior PCI	63 (17.4)	10 (5.4)	53 (29.6)	<0.001
BSA	1.9 ± 0.3	1.9 ± 0.4	2 ± 0.3	0.017
NYHA functional class at initial TAVR				0.003
1	9 (2.7)	2 (1.2)	7 (4.1)	
2	73 (22.0)	29 (17.9)	44 (25.9)	
3	197 (59.3)	112 (69.1)	85 (50.0)	
4	53 (16.0)	19 (11.7)	34 (20.0)	
Previous cardiac surgery	135 (38.4)	47 (27.2)	88 (49.2)	<0.001
STS PROM, %	3.2 (2.2-5.1)	3.5 (2.3-5.8)	3.1 (2.1-4.9)	0.11
Heart team risk stratification				<0.001
Low	36 (14.3)	8 (7)	28 (20.6)	
Intermediate	91 (36.3)	34 (29.6)	57 (41.9)	
High	104 (41.4)	61 (53)	43 (31.6)	
Extreme	20 (8)	12 (10.4)	8 (5.9)	

Values are mean ± SD, n (%), or median (IQR).

BSA = body surface area; ICD = implantable cardioverter-defibrillator; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; TAVR-explant = transcatheter aortic valve replacement surgical explantation.

reintervention, and compared between the redo-TAVR and TAVR-explant groups. Continuous variables were reported as mean ± SD or median (IQR) depending on distribution of data, whereas categorical variables are reported as frequencies and proportions. Assessment of normality for continuous data was performed using the Kolmogorov-Smirnov test. Depending on distribution of data, differences between redo-TAVR and TAVR-explant groups were detected using the Student 2-sample *t*-test or Mann-Whitney *U* test for continuous variables, and chi-square or Fisher exact test for categorical variables.

Differences in actuarial all-cause mortality were assessed using Kaplan-Meier analysis according to type of reintervention (ie, redo-TAVR or TAVR-explant), and initial THV type (balloon-expandable valve [BEV] and non-BEV [self-expanding/mechanically expandable valves]). Given the likelihood of higher perioperative mortality in the TAVR-explant group, landmark analysis was performed beginning at 30 days after the reintervention. Risk factors for 30-day and 1-year all-cause mortality were assessed using univariate logistic regression analysis. Because model building was limited by the relative number of mortality events, only forward, stepwise, multivariable Cox regression models were developed. Candidate variables were chosen based on statistical significance on univariate analysis ($P < 0.10$) and a priori clinical relevance to the outcomes of interest. Collinearity between variables was assessed using the variance inflation factor test, and those with values >2.5 were not included in the multivariable model; if highly collinear variables were substantially associated with the outcomes of interest, the variable that best improved the predictive performance was included. A 2-sided $P < 0.05$ was considered statistically significant, and all statistical analyses were performed using SPSS version 24.0 (IBM).

RESULTS

BASELINE CLINICAL CHARACTERISTICS AT INDEX TAVR. Among 66,760 patients undergoing TAVR at the sites participating in the EXPLANTORREDO-TAVR registry during the study period, a total of 396 (0.59%) patients underwent reintervention for THV failure, per the inclusion criteria. Baseline clinical characteristics at the index-TAVR procedure are summarized in Table 1. Mean age was 75.5 ± 9.3 years, 40.9% were female, and 14.3% of patients were deemed low surgical risk by the local heart team. At index-TAVR, 38.4% of patients had previous cardiac surgery, and 75.3% had NYHA (New York Heart Association) functional class III/IV symptoms. Median Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) for surgical aortic valve replacement (SAVR) was 3.2% (IQR: 2.2%-5.1%) at index-TAVR, and increased to 4.6% (IQR: 2.7%-7.7%; $P < 0.001$) at subsequent reintervention. Compared with TAVR-explant, redo-TAVR had similar STS PROM at index-TAVR (3.5% [IQR: 2.3%-5.8%] vs 3.1% [IQR: 2.1%-4.9%]; $P = 0.11$) and reintervention (5.1% [IQR: 2.9%-8.0%] vs 3.9% [IQR: 2.5%-6.6%]; $P = 0.10$). Redo-TAVR patients were older at the time of index-TAVR procedure (78.6 ± 8.4 years vs 72.1 ± 9.0 years; $P < 0.001$), with greater surgical risk as determined by the heart

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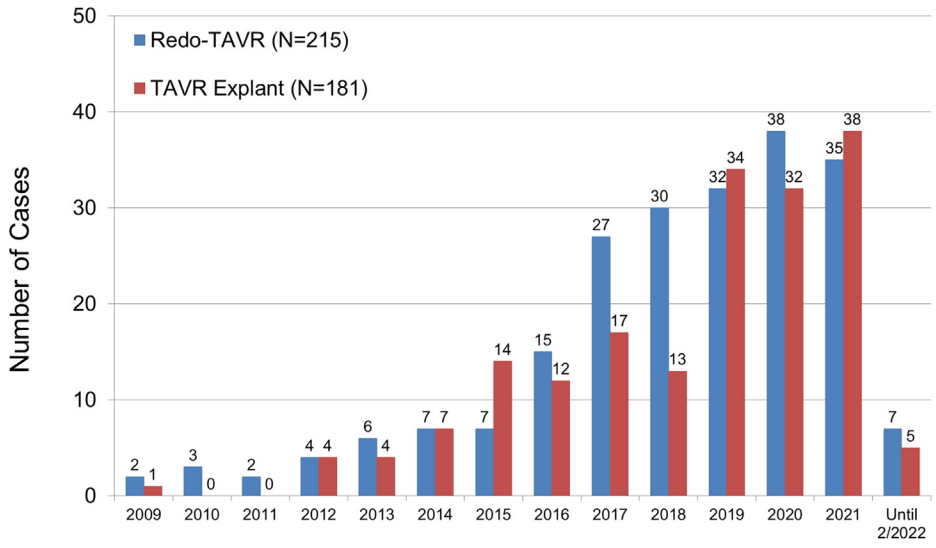
FIGURE 2 **Temporal Trends in Annual Reinterventions for Failed TAVR**



Trends in the annual number of redo-TAVR and TAVR-explant for failed TAVR between 2009-2022 in the EXPLANTORREDO-TAVR International Registry. Abbreviations as in Figure 1.

team (high/extreme risk: 63.4% vs 37.5%; $P < 0.001$), and more calcified aorta (24.5% vs 6.4%; $P < 0.001$). TAVR-explant had more prior percutaneous coronary intervention (29.6% vs 5.4%; $P < 0.001$) and previous cardiac surgery (49.2% vs 27.2%; $P < 0.001$) compared with redo-TAVR. Temporal trends in annual TAVR-explant and redo-TAVR in the EXPLANTORREDO-TAVR registry are shown in Figure 2.

CHARACTERISTICS OF THV FAILURE. The median interval from index-TAVR to reintervention for THV failure was 31.5 months (IQR: 6.5-60.3 months). Compared with redo-TAVR, the TAVR-explant group had a shorter median interval from index-TAVR to reintervention (17.6 months [IQR: 5.0-40.7 months] vs 45.7 months [IQR: 10.6-75.6 months]; $P < 0.001$) (Central Illustration). Indications for reintervention included SVD (58.2%), PVL (30.9%), severe PPM (8.3%), delayed THV migration (1.8%), and THV thrombosis (2.9%) (Table 2), with >1 indication for reintervention present in 33 patients (8.6%). There were more SVD in redo-TAVR (63.7% vs 51.9%; $P = 0.023$), whereas TAVR-explants were more likely to have severe PPM (17.1% vs 0.5%; $P < 0.001$) or delayed valve migration (3.3% vs 0.5%; $P = 0.055$). There were similar proportions of ≥moderate PVL (32.8% redo-TAVR vs 28.7% TAVR-explant; $P = 0.44$) and THV thrombosis (3.9% redo-TAVR vs 1.7% TAVR-explant; $P = 0.23$) between groups. In patients undergoing TAVR-explant, the primary reasons reported for exclusion from redo-TAVR in addition to the aforementioned indications for TAVR-explant were unfavorable anatomy (19.3%) and prior transcatheter aortic valve-in-valve replacement (6.6%). Unfavorable anatomy as a reason for TAVR-explant was defined by high risk of coronary obstruction with redo-TAVR as described previously.[10]

PROCEDURAL CHARACTERISTICS ON REINTERVENTION. Urgent/emergency cases comprised 29.3% of all reinterventions, with more such cases in the TAVR-explant group (38.6% vs 20.8%; $P < 0.001$) (Table 3). Aortic root replacement was performed in 10.5% of patients undergoing TAVR-explant, of which 10.5% received mechanical valves and 89.5% received bioprosthetic valves. In the remaining 89.5% undergoing SAVR without root replacement, mechanical valves were implanted in 14.2%, and 85.8% received bioprosthetic valves. The decision to use mechanical valves was based on surgeon and patient preference. Concomitant cardiac procedures during TAVR-explant were performed in 55.8% of patients, including ascending aortic replacement (6.1%), coronary artery bypass grafting (17.7%), mitral valve surgery (20.4%), tricuspid valve surgery (2.8%), and aortic root repair (1.7%). Median cardiopulmonary

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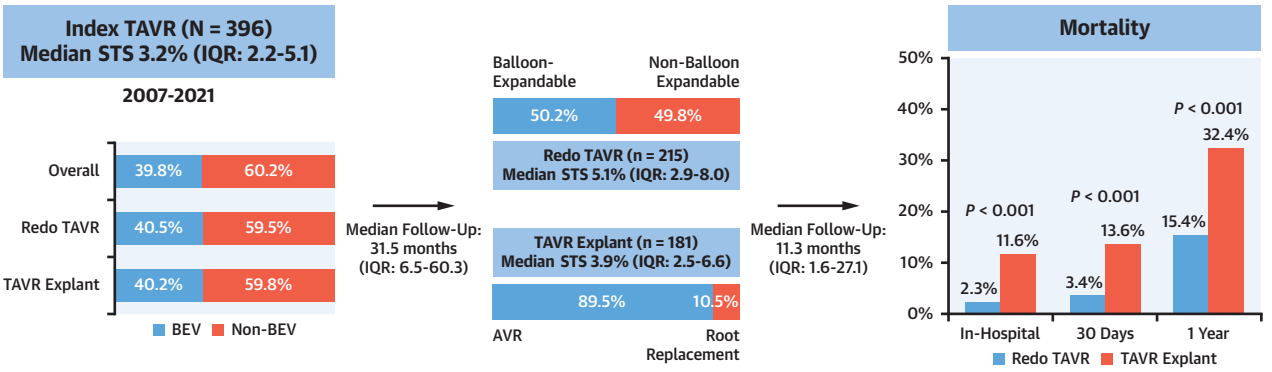
CENTRAL ILLUSTRATION Summary of the EXPLANTORREDO-TAVR International Registry

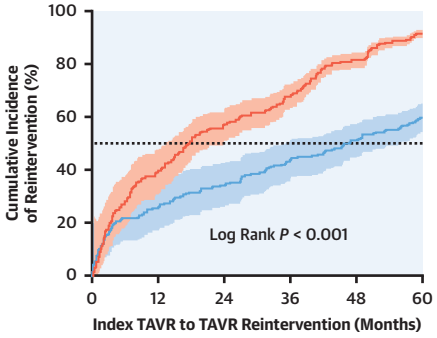
Explant Versus Redo TAVR After THV Failure: Outcomes From the EXPLANTORREDO-TAVR International Registry: 29 Paired Centers, N = 396



Mechanism of TAVR Failure

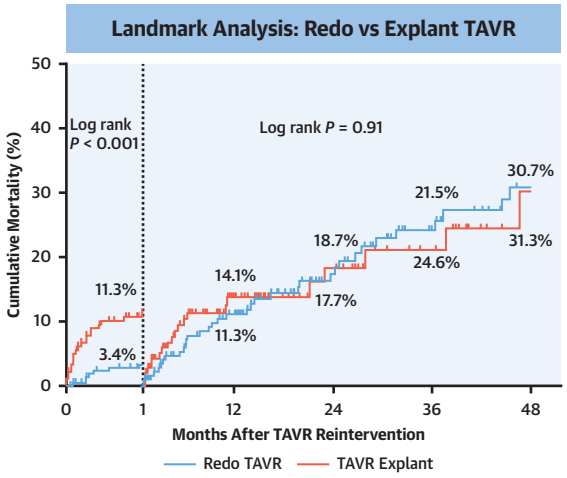
	Redo TAVR	TAVR Explant	*P* Value
SVD	63.7%	51.9%	0.023
PVL	32.8%	28.7%	0.44
PPM	0.5%	17.1%	<0.001
THV Thrombosis	3.9%	1.7%	0.23
THV Migration	0.5%	3.3%	0.055

Time to TAVR Reintervention



	Redo TAVR	TAVR Explant	*P* Value
Median Interval (months)	45.7 (IQR: 10.6-75.6)	17.6 (IQR: 5.0-40.7)	<0.001

Landmark Analysis: Redo vs Explant TAVR



Tang GHL., et al. J Am Coll Cardiol Intv. 2023;16(8):927-941.

AVR = aortic valve replacement; BEV = balloon-expandable valve; PPM = prosthesis-patient mismatch; PVL = paravalvular leak; STS = Society of Thoracic Surgeons; SVD = structural valve degeneration; TAVR = transcatheter aortic valve replacement; THV = transcatheter heart valve.

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bypass and cross-clamp times were 146 (IQR: 106-202) minutes and 104 (IQR: 73-149) minutes, respectively.

IMPACT OF THV TYPE ON REINTERVENTION. Overall, BEV and non-BEV failures accounted for 40.2% and 59.8% of the reinterventions, respectively (Table 3). There were no differences in reintervention strategy for BEV failure (54.7% redo-TAVR vs 45.3% TAVR-explant; $P = 0.92$) or non-BEV failure (54.0% redo-TAVR vs 46.0% TAVR-explant; $P = 0.92$). However, within the BEV-failure cohort, redo-TAVR was more common than TAVR-explant for SAPIEN XT (Edwards Lifesciences) failure (46.0% vs 19.4%, respectively; $P < 0.001$), and less common for SAPIEN 3 (Edwards Lifesciences) failure (29.9% vs 63.9%, respectively; $P < 0.001$). Similarly, within the CoreValve platform, redo-TAVR was less common for Evolut PRO/PRO+ (Medtronic) failure (5.5% vs 15.6%; $P = 0.036$). Redo-TAVR for BEV failure was preferentially treated using non-BEV (58.6% vs 41.4% BEV THV; $P = 0.038$), whereas non-BEV failure was preferentially treated with BEV (56.3% vs 43.8% non-BEV THV; $P = 0.038$) (Figure 3). Non-BEV failure trended a higher proportion of root replacement performed (13.9% vs 5.6%; $P = 0.087$), with a similar proportion of mechanical valves implanted (14.8% vs 12.5%; $P = 0.83$).

POSTPROCEDURAL AND MID-TERM CLINICAL OUTCOMES. Overall intraoperative and in-hospital mortality was 0.5% and 6.8%, respectively (Table 4). Compared with redo-TAVR, TAVR-explant had higher in-hospital mortality (11.6% vs 2.8%; $P = 0.001$), and longer median intensive care unit (72 hours [IQR: 33-150 hours] vs 5 hours [IQR: 0-24 hours]; $P < 0.001$) and hospital (11 days [IQR: 7-17 days] vs 5 days [IQR: 2-7 days]; $P < 0.001$) lengths of stay. The redo-TAVR group had 1 coronary obstruction (23-mm SAPIEN 3 for SVD in a 26-mm CoreValve), and 4 conversions (1.9%) to open surgery (2 aortic dissections and 2 planned procedures on cardiopulmonary bypass with resection of prior valve leaflets). With the exception of more vascular complications in the redo-TAVR group (12.3% vs 2.9%; $P = 0.001$), there were no differences in other periprocedural complication rates between groups. There were no differences in prosthetic mean transvalvular gradient at discharge between groups (12.2 ± 6.7 mm Hg after redo-TAVR vs 11.8 ± 5.7 mm Hg after TAVR-explant; $P = 0.67$). Compared with TAVR-explant, redo-TAVR had more moderate residual PVL (5.6% vs 0%; $P < 0.001$), but moderate central aortic regurgitation occurred with similar frequencies in both groups (2.8% vs 0%; $P = 0.30$).

At 30-day follow-up, mortality was 8.0%, whereas stroke and readmission rates were 3.4% and 13.8%, respectively. Among patients who completed 1-year follow-up, mortality was 22.3% and stroke rate was 5.3%. Stroke rates were similar between the 2 groups at 30 days (4.2% redo-TAVR vs 2.4% TAVR-explant; $P = 0.40$) and 1 year (5.8% vs 4.6%; $P = 0.78$). The median follow-up duration was 13.6 months (IQR: 2.4-35.9 months) from redo-TAVR and 6.7 months (IQR: 1.3-15.9) months from TAVR-explant procedure. Compared with redo-TAVR, TAVR-explant had higher mortality at 30 days (13.6% vs 3.4%; $P < 0.001$) and 1 year (32.4% vs 15.4%; $P = 0.001$). TAVR-explant had higher cumulative mortality compared with redo-TAVR ($P = 0.049$) (Figure 4). However, actuarial estimates of mortality at 3 years were 27.1% in redo-TAVR and 30.4% in TAVR-explant. Landmark analysis at 30 days showed higher 30-day mortality in the TAVR-explant group ($P < 0.001$), but similar rates between groups after 30 days ($P = 0.91$). When examining 1-year mortality by the reintervention era—before and after 2016 through 2019—no significant differences were observed between time periods in 1-year mortality with either redo-TAVR or TAVR-explant (Supplemental Figure S2). Survival analysis after reintervention stratified by index-TAVR type also did not reveal any significant differences in cumulative mortality between BEV vs non-BEV THV failure undergoing redo-TAVR ($P = 0.83$) or TAVR-explant ($P = 0.49$) (Supplemental Figure S3).

TABLE 2 Indications for Reintervention

	Overall (N = 396)	Redo-TAVR (n = 215)	TAVR-Explant (n = 181)	*P* Value
Structural valve degeneration	224 (58.2)	130 (63.7)	94 (51.9)	0.023
Paravalvular leak	119 (30.9)	67 (32.8)	52 (28.7)	0.44
Prosthesis–patient mismatch	32 (8.3)	1 (0.5)	31 (17.1)	<0.001
Prosthetic valve thrombosis	11 (2.9)	8 (3.9)	3 (1.7)	0.23
Delayed valve migration	7 (1.8)	1 (0.5)	6 (3.3)	0.055

Values are n (%).
TAVR = transcatheter aortic valve replacement.

PREDICTORS OF ALL-CAUSE MORTALITY AFTER REINTERVENTION. On univariate analysis, 1-year mortality after redo-TAVR was associated with STS PROM at index-TAVR, heart team-determined risk at index-TAVR, diabetes, stroke, dialysis, STS PROM at redo-TAVR, and new permanent pacemaker implantation (Figure 5A). After adjusting for significant univariates and relevant clinical factors on multivariable Cox regression, independent predictors of mortality after redo-TAVR were found to be chronic kidney disease (CKD; HR: 4.11 [95% CI: 1.85-9.15]), heart team-determined risk at redo-TAVR (HR: 2.16 [95% CI: 1.24-3.77]) and urgent/emergent redo-TAVR

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TABLE 3 Procedural Characteristics at the Time of Reintervention

	Overall (N = 396)	Redo-TAVR (n = 215)	TAVR-Explant (n = 181)	*P* Value
STS PROM at TAVR reintervention, %	4.6 (2.7-7.7)	5.1 (2.9-8.0)	3.9 (2.5-6.6)	0.10
Timing of operation				
Elective	234 (70.7)	137 (79.2)	97 (61.4)	<0.001
Urgent	84 (25.4)	30 (17.3)	54 (34.2)	0.001
Emergent	13 (3.9)	6 (3.5)	7 (4.4)	0.78
Failed TAVR size, mm	26 (23-29)	26 (23-29)	26 (23-29)	
TAVR device type at failure				0.92
Balloon-expandable	159 (40.2)	87 (40.5)	72 (39.8)	
SAPIEN	33 (20.8)	21 (24.1)	12 (16.7)	<0.001
SAPIEN XT	54 (34)	40 (46)	14 (19.4)	
SAPIEN 3	72 (45.3)	26 (29.9)	46 (63.9)	
Self-expanding/mechanically expandable	237 (59.8)	128 (59.5)	109 (60.2)	
CoreValve	103 (43.5)	60 (46.9)	43 (39.4)	0.036
Evolut R	55 (23.2)	30 (23.4)	25 (22.9)	
Evolut PRO/PRO+	24 (10.1)	7 (5.5)	17 (15.6)	
ACURATE-neo	16 (6.8)	9 (7)	7 (6.4)	
Portico	15 (6.3)	9 (7)	6 (5.5)	
Navitor	2 (0.8)	1 (0.8)	1 (0.9)	
Lotus	10 (4.2)	6 (4.7)	4 (3.7)	
Direct Flow	5 (2.1)	2 (1.6)	3 (2.8)	
JenaValve	4 (1.7)	3 (2.3)	1 (0.9)	
Engager	3 (1.3)	1 (0.8)	2 (1.8)	
Time from initial TAVR to reintervention, mo	31.5 (6.5-60.3)	45.7 (10.6-75.6)	17.6 (5.0-40.7)	<0.001
Implanted valve size, mm	25 (23-27)	26 (23-29)	23 (23-25)	
Balloon-expandable		108 (50.2)		
SAPIEN		2 (1.9)		
SAPIEN XT		2 (1.9)		
SAPIEN 3		104 (96.3)		
Self-expanding/mechanically expandable		107 (49.8)		
CoreValve		22 (20.6)		
Evolut R		52 (48.6)		
Evolut PRO/PRO+		22 (20.6)		
ACURATE-neo		0 (0)		
Portico		4 (3.7)		
Navitor		0 (0)		
Lotus		3 (2.8)		
Direct Flow		0 (0)		
JenaValve		0 (0)		
Engager		0 (0)		
Allegra		4 (3.7)		
Cardiopulmonary bypass time, min			146 (106-202)	
Aortic cross-clamp time, min			104 (73-149)	
Aortic valve replacement			162 (89.5)	
Mechanical			23 (14.2)	
Tissue			139 (85.8)	
Root replacement			19 (10.5)	
Mechanical			2 (10.5)	
Tissue			17 (89.5)	
Concomitant procedure(s)[a]			101 (55.8)	
Ascending aortic replacement			11 (6.1)	
CABG			32 (17.7)	
Mitral valve surgery			37 (20.4)	
Tricuspid valve surgery			5 (2.8)	
Mitral/tricuspid valve surgery			42 (23.2)	
Root repair			3 (1.7)	
Root enlargement			30 (16.6)	
Ascending aortic graft size			28 (26-30)	

Values are median (IQR) or n (%). [a]Other concomitant procedures include ventricular septal defect repair, ventricular assist device placement, Ross, and heart transplantation, among others.

CABG = coronary artery bypass grafting; other abbreviations as in Table 1.

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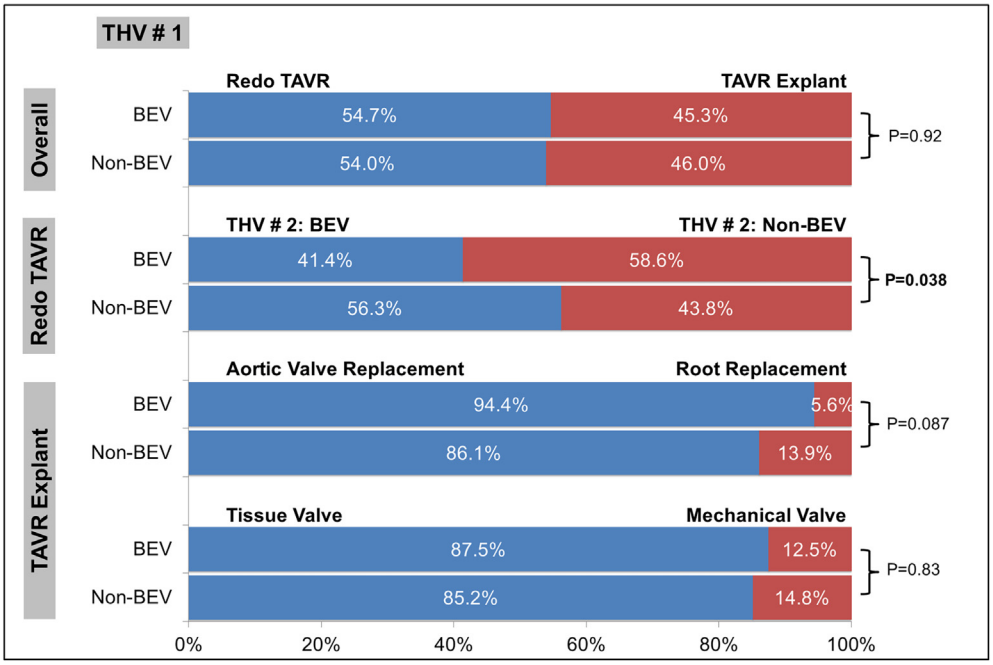
FIGURE 3 **Reintervention Stratified by Type of Initial TAVR**



Implanted valve types at Reintervention stratified by initial TAVR type, as balloon-expandable valve (BEV) vs non-BEV (self-expanding/mechanically expandable valve) failure. Overall, there were no differences between BEV vs non-BEV failure in patients who underwent redo-TAVR (54.7% for BEV failure vs 54.0% for non-BEV failure; $P = 0.92$) and TAVR-explant (45.3% for BEV failure vs 46.0% for non-BEV failure; $P = 0.92$). Redo-TAVR for BEV failure was preferentially treated with non-BEV (58.6% vs 41.4% BEV THV; $P = 0.038$), whereas non-BEV failure was preferentially treated with BEV (56.3% vs 43.8% non-BEV THV; $P = 0.038$). Compared with TAVR-explant for BEV failure, non-BEV failure had numerically higher proportion of root replacement performed (13.9% vs 5.6%; $P = 0.087$), with similar proportion of mechanical valves implanted (14.8% vs 12.5%; $P = 0.83$). Abbreviations as in **Figure 1**.

(HR: 3.21 [95% CI: 1.35-7.65]). Similarly, 1-year mortality after TAVR-explant was associated with younger age, diabetes, peripheral vascular disease, CKD, STS PROM at TAVR-explant, and cardiopulmonary bypass time (**Figure 5B**). Independent predictors of all-cause mortality after TAVR-explant were dialysis (HR: 3.30 [95% CI: 1.42-7.68]), pulmonary hypertension (HR: 2.34 [95% CI: 1.22-4.50]), and concomitant mitral surgery at TAVR-explant (HR: 2.34 [95% CI: 1.17-4.66]). Mortality after redo-TAVR or TAVR-explant was not associated with mechanism of THV failure, type of THV failure (BEV vs non-BEV failure), or type of valve implanted (BEV vs non-BEV with redo-TAVR, or mechanical vs bioprosthetic valve with TAVR-explant). In a multivariable Cox regression model that included both the redo-TAVR and TAVR-explant cohorts, TAVR-explant (compared with redo-TAVR) was not independently associated with mortality after reintervention for THV failure (HR: 1.34 [95% CI: 0.79-2.28]; $P = 0.28$) (Supplemental Table S1).

DISCUSSION

This multicenter, international EXPLANTORREDO-TAVR registry is the first study to report the incidence, characteristics, and mid-term outcomes of TAVR-explant and redo-TAVR across the same centers. This is the largest and most comprehensive in-depth evaluation to date comparing the 2 treatment strategies for THV failure. The incidence of AV reintervention after THV failure was 0.59%. Our study has several key findings (**Central Illustration**): First, the incidence of reintervention after THV failure was low at 0.59%, but there was a rising trend during the study period. Second, in terms of mechanism of THV failure, redo-TAVR patients had more SVD, but a lower frequency of PPM or delayed valve migration.

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TABLE 4 Outcomes After Reintervention

	Overall (N = 396)	Redo-TAVR (n = 215)	TAVR-Explant (n = 181)	*P* Value
Intraprocedural mortality	2 (0.5)	0 (0)	2 (1.1)	0.21
In-hospital mortality	27 (6.8)	6 (2.8)	21 (11.6)	0.001
ICU length-of-stay, h	25.5 (4.3-86.5)	5.0 (0-24.0)	72.0 (32.9-150.0)	<0.001
Hospital length-of-stay, d	7 (4-13)	5 (2-7)	11 (7-17)	<0.001
New left bundle branch block[a]	24 (9.3)	16 (12)	8 (6.5)	0.14
New permanent pacemaker[a]	42 (14.1)	18 (11.1)	24 (17.8)	0.13
In-hospital stroke	10 (2.7)	6 (3)	4 (2.3)	0.76
Coronary obstruction	1 (0.3)	1 (0.5)	0 (0)	1.0
Conversion to surgery		4 (1.9)		
In-hospital vascular complication	30 (7.9)	25 (12.3)	5 (2.9)	0.001
In-hospital life-threatening bleed	14 (4)	5 (2.9)	9 (5.2)	0.41
In-hospital major bleed	38 (10.1)	18 (8.8)	20 (11.5)	0.40
Echocardiographic Characteristics	**(N = 232)**	**(n = 143)**	**(n = 89)**	
Paravalvular leak				<0.001
None/trace	196 (84.5)	107 (74.8)	89 (100)	
Mild	28 (12.1)	28 (19.6)	0 (0)	
Moderate	8 (3.4)	8 (5.6)	0 (0)	
Central aortic regurgitation				0.49
None/trace	220 (94.8)	133 (93.0)	87 (97.8)	
Mild	8 (3.4)	6 (4.2)	2 (2.2)	
Moderate	4 (1.7)	4 (2.8)	0 (0)	
Mean gradient, mm Hg	12.0 ± 6.4	12.2 ± 6.7	11.8 ± 5.7	0.67
Peak gradient, mm Hg	22.8 ± 11.4	22.7 ± 11.9	22.8 ± 10.1	0.97
30-d				
Mortality	30 (8)	7 (3.4)	23 (13.6)	<0.001
Stroke	12 (3.4)	8 (4.2)	4 (2.4)	0.40
Readmission	41 (13.8)	19 (13.1)	22 (14.4)	0.87
1-y				
Mortality	61 (22.3)	25 (15.4)	36 (32.4)	0.001
Stroke	13 (5.3)	8 (5.8)	5 (4.6)	0.78

Values are n (%), median (IQR), or mean ± SD. [a]Patients with prior pacemaker or implantable cardioverter defibrillator were excluded.
ICU = intensive care unit; MSOF = multisystem organ failure; other abbreviations as in Table 1.

Rates of PVL and valve thrombosis were similar between groups. Third, patients undergoing TAVR-explant had a shorter median time to reintervention compared with redo-TAVR. Fourth, there were no differences in distribution of BEV vs non-BEV failure between redo-TAVR and TAVR-explant. Fifth, compared with redo-TAVR, TAVR-explant had higher in-hospital mortality, and higher mortality at 30 days and 1 year. Landmark analysis at 30 days, however, showed no subsequent differences in mortality between redo-TAVR and TAVR-explant after 30 days. Finally, on multivariable analysis, CKD, heart team-determined risk at redo-TAVR and urgent/emergency procedure were independent risk factors of mortality after redo-TAVR. Dialysis, pulmonary hypertension, and concomitant mitral surgery were independent risk factors of mortality after TAVR-explant. Although these findings are hypothesis-generating, they also provide valuable insight regarding the lifetime management of severe aortic stenosis and THV failure.

RATES OF REINTERVENTION AFTER THV FAILURE REMAIN LOW BUT ARE INCREASING. Thus far, reintervention after THV failure remains a rare phenomenon, with reported frequencies of redo-TAVR between 0.33% and 0.46%,[3,4] whereas TAVR-explant incidence is 0.2% to 0.4%.[6,11] In a recent study of over 250,000 TAVR performed from 2013-2019 in the TVT Registry (Transcatheter Valve Therapy Registry), there were only 404 total AV reinterventions reported at 1 year.[12] However, there is a rising trend with >100 of these cases performed in 2019. Unfortunately, these studies were limited by either only short-term

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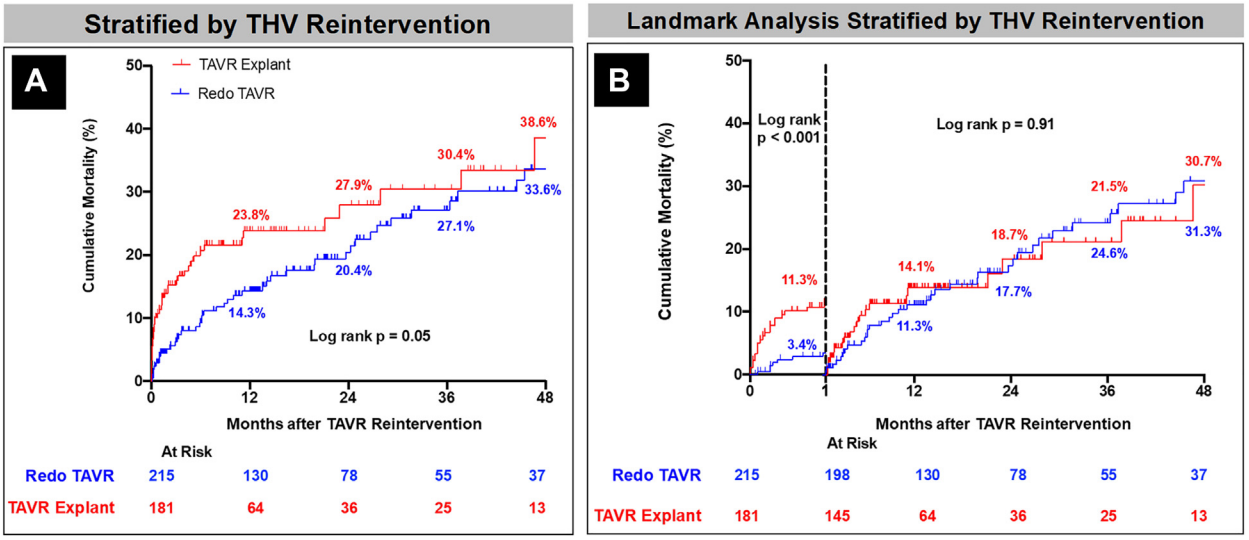
FIGURE 4 Kaplan-Meier Analysis for All-Cause Mortality After Reintervention for Failed TAVR



(A) At median follow-up of 11.3 months (IQR: 1.6-27.1 months) after reintervention, TAVR-explant had higher cumulative mortality compared with redo-TAVR ($P = 0.049$). **(B)** Landmark analysis at 30 days showed higher 30-day mortality in the TAVR-explant group ($P < 0.001$), but similar rates between groups after 30 days ($P = 0.91$). Abbreviations as in Figure 1.

(up to 1 year) follow-up, combined acute and delayed reintervention, or only 1 of the 2 treatment options evaluated. Our study reflected a similar incidence of 0.59% AV reintervention rate for THV failure but excluded patients who had acute reintervention (redo-TAVR or TAVR-explant) and those who required TAVR-explant for endocarditis. Therefore, we believe our study represents a more realistic longitudinal picture of AV reintervention after THV failure, even though the true incidence of AV reintervention is difficult to capture. Patients who had initial TAVR at sites participating in the registry might have been reintervened elsewhere and vice versa, as well as those who declined or were not offered reintervention were not captured systematically. TAVR has now been expanded to lower risk and younger patients. Since these patients have longer life expectancies, and possibly earlier SVD, as has been observed in surgical valves, there is likely to be an increasing need for subsequent intervention following THV failure. Indeed, the current study documented a rising trend of AV reintervention as have several others.[1,4,12] Accordingly, we need to be prepared to manage the increasing incidence of THV failure requiring reintervention.

RATES OF TAVR-EXPLANT SIMILAR TO REDO-TAVR BUT WITH DIFFERENT MECHANISMS OF THV FAILURE. Our study offers the unique insight into heart team decisions concerning reintervention strategy after THV failure. Interestingly, the overall rates of TAVR-explant and redo-TAVR were similar (45.7% vs 54.3%). This differs from the PARTNER (Placement of Aortic Transcatheter Valve) 2A trial, where the 5-year AV reintervention rate was 3.2%, of whom 81% had redo-TAVR, whereas 14.3% had TAVR-explant.[13] However, the mechanism of THV failure was not detailed in the PARTNER 2A study. In our study, the predominant indication favoring redo-TAVR was SVD, whereas the leading indication favoring TAVR-explant was PPM; PVL and valve thrombosis as indications were similar between the 2 treatments. The former difference seems rational, given that redo-TAVR would generally be preferred when expected hemodynamic outcomes would be favorable, given its less invasive approach. TAVR-explant only would be preferable in operable patients where redo-TAVR was anatomically unfeasible or would have led to a suboptimal hemodynamic result, as shown in our EXPLANT-TAVR registry.[1] Unfortunately, unlike balloon valve fracture or remodeling, which may minimize PPM after TAVR in failed surgical bioprostheses, there is no similar technique to address PPM after TAVR. TAVR-explant, therefore, remains the only option in reintervention. Given that 17.1% of TAVR-explant cases were due to PPM, operators should aim to minimize such incidence during initial TAVR, particularly in patients whose long-term

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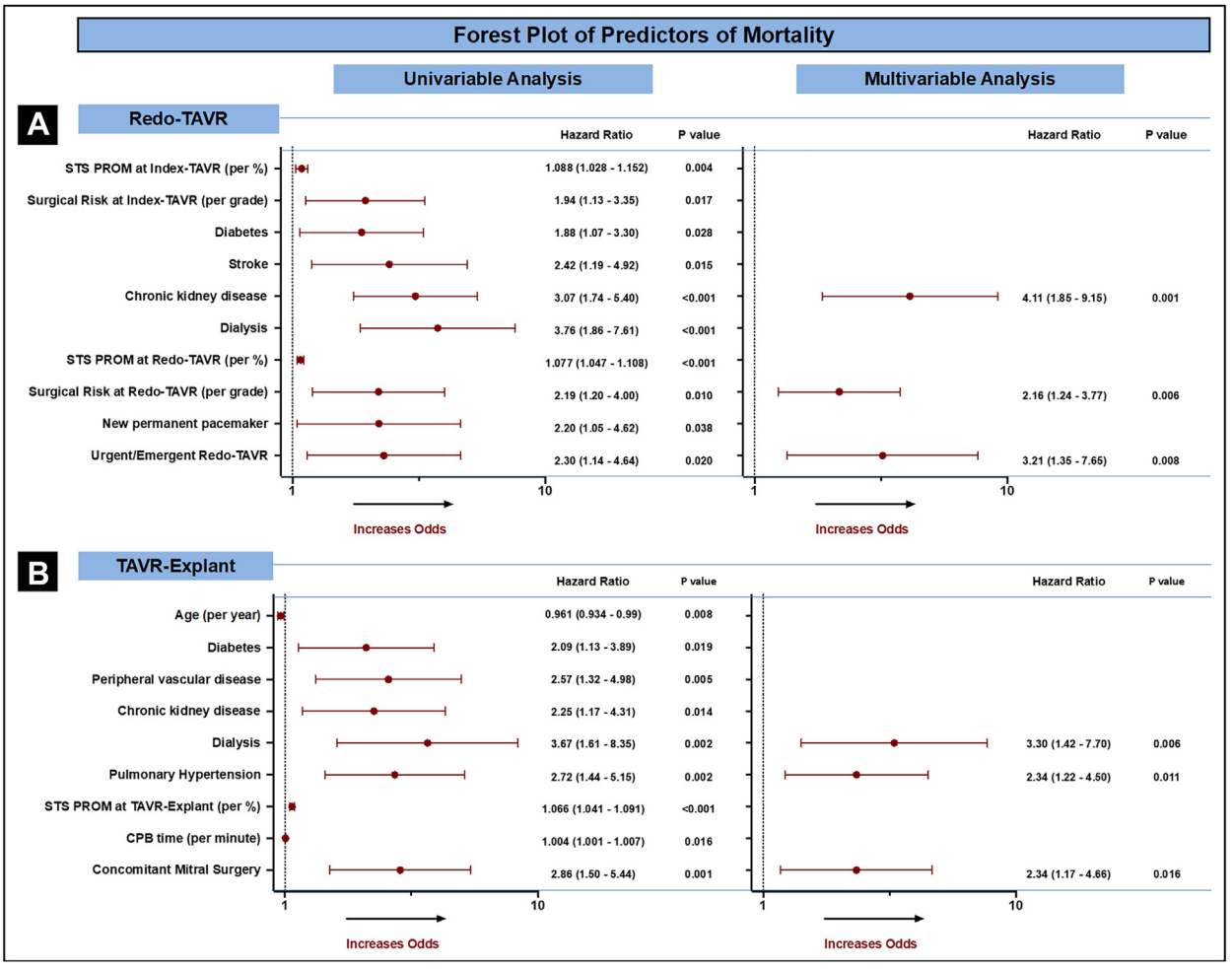
FIGURE 5 Forest Plot of Predictors of All-Cause 1-Year Mortality After Reintervention



Forest plot showing univariable and multivariable predictors of all-cause 1-year mortality after redo-TAVR **(A)** and TAVR-explant **(B)**. CPB = cardiopulmonary bypass; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; other abbreviations as in Figure 1.

survival suggests that they are likely to require AV reintervention. By the same token, we should aim to minimize PVL after initial TAVR, given it represented 30.9% of the indication for AV reintervention. Accordingly, meticulous periprocedural echocardiographic interrogation and careful consideration of prosthesis design and implant depth are especially critical in lower-risk and younger patients. Redo-TAVR may improve PVL, but in our study, 25.2% remained at mild or greater PVL after reintervention, which may have long-term adverse sequelae.

DIFFERENT TIMING OF REINTERVENTION BETWEEN REDO-TAVR AND TAVR-EXPLANT LIKELY MULTIFACTORIAL. One of the more interesting findings in our study was that the time interval from initial TAVR to TAVR-explant was shorter than the interval to redo-TAVR. The likely explanation is multifactorial. First, redo-TAVR patients were older with higher surgical risks, so even with evidence of THV failure, the heart team might have been less inclined to commit to earlier reintervention. Second, the indications for reintervention suggest greater clinical acuity (ie, delayed THV migration, severe PPM, and significant PVL not amenable to percutaneous intervention), hence the only treatment option would be TAVR-explant. Such patients would likely have significant symptoms, necessitating earlier surgical intervention. As we have found in the EXPLANT-TAVR registry, those who underwent TAVR-explant were at higher surgical risk compared with the surgical risk at the time of initial TAVR

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(median STS PROM increased from 3.2% to 5.1%). Therefore, there might be an impetus to intervene sooner, before the patients became too high risk for surgery. TAVR-explant may also potentially be easier earlier after index-TAVR, before tissue ingrowth makes it harder to remove the THV.

STRATEGY AND OUTCOMES OF AV REINTERVENTION SIMILAR BETWEEN BEV VS NON-BEV. Recent reports by Landes et al[14] and Fukuhara et al[15] showed that the initial THV type did not have a significant impact on outcomes after AV intervention for THV failure. Although TAVR-explant with prior self-expanding THV had more frequent aortic root and ascending aortic replacement, this was not associated with increased mortality.[16,17] In the current study, patients who underwent redo-TAVR and TAVR-explant had similar rates of BEV and non-BEV failure. However, unlike the observations by Landes et al,[14] we saw more BEV use in failed non-BEV and vice versa in the redo-TAVR group. Currently, only BEV is approved in the United States for redo-TAVR. Further analyses will be necessary to determine the relationship between failure in the THV type and AV reintervention strategy in our study.

REDO-TAVR WAS LESS RISKY THAN TAVR-EXPLANT BUT PROGNOSIS REMAINED SIMILAR. Consistent with findings by Percy et al,[4] we found the 30-day mortality was higher in the TAVR-explant compared with the redo-TAVR group. Although their study showed similar 1-year mortality at ~21%, ours showed a persistent higher 1-year mortality in the TAVR-explant group, and only after landmark analysis beyond 30 days was the mortality similar between the 2 groups. Clearly, the 2 groups have different baseline characteristics with inherent selection bias demonstrating the differences in early outcomes. It was important to see that if patients survived TAVR-explant beyond 30 days, then their prognosis became similar to those who had undergone redo-TAVR, with 4-year mortality ~30% after landmark analysis. Given our study cohort were patients who had reintervention, this might compare favorably to the 5-year mortality of >40% in intermediate surgical risk patients who underwent initial TAVR or SAVR in the PARTNER 2A trial.[13]

Although the predictors for 1-year mortality in both redo-TAVR and TAVR-explant were mostly due to patient risk profile, underlying comorbidities and urgency of their procedures, concomitant mitral surgery during TAVR-explant was predictive of increased mortality. Progressive mitral valve disease after initial TAVR could be due to primary mitral pathology that was not addressed with TAVR alone, or likely, deep THV implantation leading to anterior leaflet dysfunction and fibrosis. In lower surgical risk patients with concomitant aortic and primary mitral valve diseases, double valve surgery may be a reasonable alternative to isolated TAVR, and optimal initial THV implantation to avoid late mitral valve dysfunction necessitating subsequent TAVR-explant and mitral surgery would be prudent.

STUDY LIMITATIONS. Despite the strengths of our multicenter international registry-based study, it is a retrospective observational analysis with inherent limitations. First, not all imaging data were available for analysis, and data were not core lab–adjudicated. Second, the retrospective nature of this study and a long study period may have introduced time selection and learning curve biases. Third, the primary indication for reintervention was assessed independently by the respective heart teams at each institution, and decision to perform redo-TAVR vs TAVR-explant was at the discretion of the local heart team, which may have introduced patient selection biases. Fourth, although the granularity of the database was robust, and we were able to determine the exact causes of THV failure, we were unable to account for the potential impact of procedural volume and operator/center-level variations in transcatheter and surgical techniques on clinical outcomes. Fifth, this study was not designed to determine the true incidence of THV failure requiring reintervention, and the volume of TAVR procedures performed outside participating centers referred to our participating sites for reintervention was not captured. Sixth, we were unable to account for patients who were considered for, but did not undergo or declined, reintervention, or for those who died before needing reintervention. Finally, we recognize that the redo-TAVR and TAVR-explant groups are fundamentally different. Our study findings remain hypothesis-generating, and further in-depth subgroup analyses are ongoing.

CONCLUSIONS

This first report of the multicenter, international EXPLANTORREDO-TAVR registry provides a timely longitudinal review of the incidence, characteristics, and mid-term outcomes of redo-TAVR vs TAVR-explant across the same centers. Although TAVR-explant was riskier, with earlier reintervention and higher 30-day mortality, long-term prognosis remained similar to redo-TAVR patients. Our study provides valuable insights on lifetime management of patients with THV failure, and for further research to improve these outcomes.

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Dr Mack has served as coprimary investigator for the PARTNER trial for Edwards Lifesciences and the COAPT trial for Abbott; and has served as study chair for the APOLLO trial for Medtronic. Dr Reardon has been a consultant for Medtronic, Boston Scientific, Abbott, and W. L. Gore & Associates. Dr Sathananthan has received speaker fees from Edwards Lifesciences, Medtronic, NVT Medical, and Boston Scientific; and has been a consultant for Edwards Lifesciences, Boston Scientific, Medtronic, and Anteris. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? Although TAVR expands to younger, lower-risk patients with longer life expectancies, valve reintervention after THV failure has not been studied in detail.

WHAT IS NEW? Compared with redo-TAVR for THV failure, TAVR explantation is riskier with earlier reintervention and higher 30-day mortality, but similar mid-term prognosis after landmark analysis.

WHAT IS NEXT? With limited data on long-term durability of THV, our EXPLANTORREDO-TAVR registry provides valuable insights on lifetime management of patients with THV failure and calls for further research to improve these outcomes.

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KEY WORDS paravalvular leak, prosthesis–patient mismatch, redo-TAVR, structural valve degeneration, surgical aortic valve replacement, TAVR explantation, transcatheter aortic valve replacement, transcatheter valve failure

APPENDIX For a supplemental table and figures, please see the online version of this paper.

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