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Incidence, Characteristics, Predictors, and Outcomes of Surgical Explantation After Transcatheter Aortic Valve Replacement

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ABSTRACT

BACKGROUND Currently, there is a paucity of information on surgical explantation after transcatheter aortic valve replacement (TAVR).

OBJECTIVES The purpose of this study was to examine the incidence, patient characteristics, predictors, and outcomes of surgical explantation after TAVR using a population-based, nationally representative database.

METHODS We analyzed the Medicare Provider profile to include all U.S. patients undergoing TAVR from 2012 to 2017. Time to surgical explant was calculated from the index TAVR discharge to surgical explantation. Post-operative survival was assessed using time-dependent Cox proportional hazard regression analysis and landmark analysis.

RESULTS The incidence of surgical explantation was 0.2% (227 of 132,633 patients), and was 0.28% and 0.14% in the early and newer TAVR era, respectively. The median time to surgical explant was 212 days, whereas 8.8% and 70.9% underwent surgical explantation within 30 days and 1 year, respectively. The primary indication for reintervention was bioprosthetic failure (79.3%). Compared with the no-explant cohort, the explant cohort was significantly younger (mean age 73.7 years vs. 81.7 years), with a lower prevalence of heart failure (55.9% vs. 65.8%) but more likely a lower-risk profile cohort (15% vs. 2.4%; all $p < 0.05$). The 30-day and 1-year mortality rates were 13.2% and 22.9%, respectively, and did not vary by either time to surgical explant or TAVR era, or between patients with versus without endocarditis (all $p > 0.05$). The time-dependent Cox regression analysis demonstrated a higher mortality in those with surgical explantation (hazard ratio: 4.03 vs. no-explant group; 95% confidence interval: 1.81 to 8.98). Indication, time-to-surgical-explant, and year of surgical explantation were not associated with worse post-explantation survival (all $p > 0.05$).

CONCLUSIONS The present study provides updated evidence on the incidence, timing, and outcomes of surgical explantation of a TAVR prosthesis. Although the overall incidence was low, short-term mortality was high. These findings stress the importance of future mechanistic studies on TAVR explantation and may have implications on lifetime management of aortic stenosis, particularly in younger patients. (J Am Coll Cardiol 2020;76:1848–59)

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Over the last decade, there has been a significant paradigm shift in the management of patients with symptomatic aortic stenosis. Transcatheter aortic valve replacement (TAVR) is now approved by the U.S. Food and Drug Administration in patients at all surgical risk profiles (1–5). Although advancements in TAVR valve technologies, refinements in procedural techniques, and use of the multidisciplinary structural heart team have contributed towards the application of percutaneous approaches in the larger population (6,7), surgical explantation of a TAVR valve is still required in certain cases. Surgical explantation of transcatheter valves after initial successful implantation remains

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rare, and existing published data is limited to only isolated small case reports or series (8–11). Furthermore, as TAVR expands to younger patients, valve reintervention is inevitable in the setting of possible structural valve deterioration (SVD), endocarditis, or significant paravalvular leak (PVL) (12,13). Currently, there is a paucity of information on the outcomes of TAVR explantation. This information is vital for understanding the impact on the lifetime management of patients who receive TAVR.

TAVR-in-TAVR has been previously reported and is a less invasive reintervention option in most patients (14,15). However, surgical explantation of the TAVR valve will be the mainstay treatment option in patients with endocarditis and in those with anatomic conditions such as coronary obstruction or significant PVL, which may preclude TAVR-in-TAVR. The aim of this nationally representative, multicenter study is to examine the incidence, patient characteristics, predictors, and outcomes of early surgical explantation after initial TAVR. This information, which is currently lacking, will provide timely benchmarking data that will help the heart team provide nuanced care in patients with aortic stenosis.

METHODS

DATA SOURCE. With permission from our Institutional Review Board, we analyzed the Medicare Provider Analysis Review and Master Beneficiary Summary File data from the Centers for Medicare and Medicaid Services (CMS) for the years 2012 through 2017 for all TAVR procedures. The International Classification of Diseases (ICD)-Clinical Modification codes used to identify TAVR procedures are presented in Supplemental Table 1. Records, where these procedures were

ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

CKD = chronic kidney disease

CMS = Centers for Medicare & Medicaid Services

HF = heart failure

ICD = International Classification of Diseases

ICU = intensive care unit

IQR = interquartile range

LOS = length of stay

PVL = paravalvular leak

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

SVD = structural valve deterioration

TAVR = transcatheter aortic valve replacement

Directors of Boston VA Research Institute, Society of Cardiovascular Patient Care, and TobeSoft; has served as chair of the American Heart Association Quality Oversight Committee, NCDR-ACTION Registry Steering Committee, and VA CART Research and Publications Committee; has served on data monitoring committees for Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi-Sankyo), and the Population Health Research Institute; has received honoraria from American College of Cardiology (Senior Associate Editor, *Clinical Trials and News*, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor-in-Chief, *Harvard Heart Letter*), Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor-in-Chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (Guest Editor; Associate Editor), Medtelligence/ReachMD (CME steering committees), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, *Cardiology Today's Intervention*), Society of Cardiovascular Patient Care (Secretary/Treasurer), and WebMD (CME steering committees); has served as Deputy Editor of *Clinical Cardiology*; has received research funding from Abbott, Afimmune, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Chiesi, CSL Behring, Eisai, Ethicon, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Idorsia, Ironwood, Ischemix, Lexicon, Lilly, Medtronic, PhaseBio, Pfizer, PLx Pharma, Regeneron, Roche, Sanofi, Synaptic, and The Medicines Company; has received royalties from Elsevier (Editor, *Cardiovascular Intervention: A Companion to Braunwald's Heart Disease*); has served as site co-investigator for Biotronik, Boston Scientific, CSI, St. Jude Medical (now Abbott), and Svelte; has served as a Trustee of the American College of Cardiology; and has performed unfunded research for FlowCo, Merck, Novo Nordisk, and Takeda. Dr. Thourani has served as an advisor and performed research for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and Jenavalve. Dr. Leon has served as a consultant for Abbott, Boston Scientific, and Medtronic; and has received research grants from Edwards Lifesciences. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. P.K. Shah, MD, served as Guest Editor-in-Chief for this paper.

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associated with diagnosis-related groups other than 216 to 221 (ICD-9) or 306, 307 (ICD-10) were excluded from this study.

PATIENT SELECTION. We included all U.S. adult patients undergoing isolated index TAVR. We excluded patients not discharged alive or those discharged to hospice after initial TAVR; those undergoing open surgical procedures, surgical explantation, or TAVR-in-TAVR during the index TAVR admission; or those who underwent TAVR-in-TAVR subsequently during the observation period (Supplemental Figure 1). The latter cohort was excluded because it represents a very unique and extremely selected cohort of patients who were eligible based on anatomic indications, as opposed to the explant cohort, who were not candidates for TAVR-in-TAVR either due to endocarditis or due to anatomic conditions. Given that these groups are inherently different by design, they likely also represent groups that would be in the extremes of propensity scores due to confounding by indication and substantial patient selection biases.

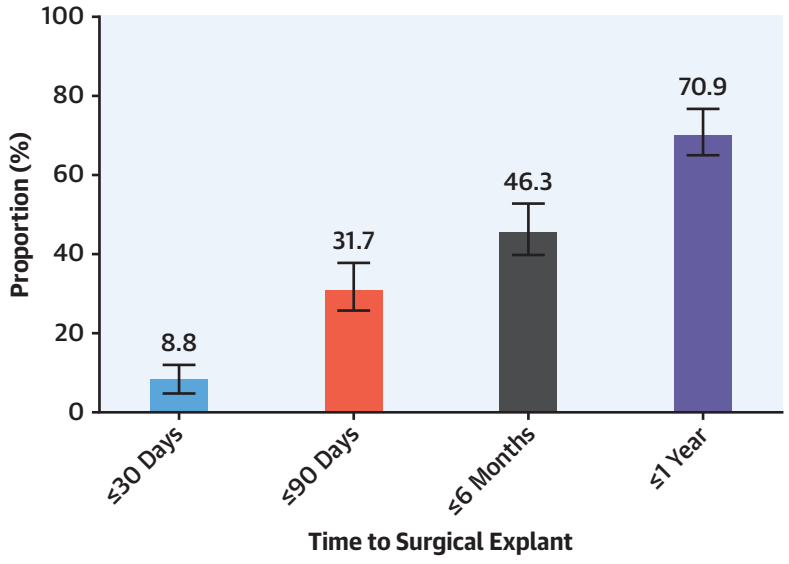
DATA COLLECTION AND DEFINITIONS. Pre-operative comorbidities and chronic conditions were derived from the Chronic Conditions file and by search of all diagnoses and procedures for those documented as present on admission or if the date of onset in the Chronic Conditions file/date of procedure was prior to the date of the admission of interest. Comorbidities derived from the Chronic Conditions file included: history of acute myocardial infarction, Alzheimer's disease, atrial fibrillation, chronic kidney disease (CKD), chronic obstructive pulmonary disease, heart failure (HF), depression, diabetes, dyslipidemia, hypertension, ischemic heart disease, osteoporosis, stroke, or transient ischemic attack. To derive post-operative complications, all diagnosis and procedure code fields were searched, and were counted when the switch field for present on admission indicated "no" or the procedure date field was after the date of the TAVR or explant procedure. Bioprosthetic failure was defined as either failed or degenerated bioprostheses based on ICD codes. However, these codes were not specific enough to differentiate between either SVD or PVL. All codes used to identify chronic conditions, comorbidities, etiology, and complications can be found in Supplemental Table 1. Time to surgical explant of TAVR valve was counted in days from the date of index TAVR discharge to the date of surgical explant. Mortality data were derived from the National Death Index. Survival time was counted in days from the date of discharge (either index TAVR or subsequent surgical explant) to mortality date or October 30, 2019, if recorded as alive.

OUTCOMES OF INTEREST. The primary outcomes of interest included the incidence of surgical explantation of TAVR valve, time to surgical explant, and 30-day and 1-year mortality. The secondary outcomes included etiology/indication for surgical explantation (endocarditis, bioprosthetic failure), bleeding complications, acute kidney injury (AKI), permanent stroke, intensive care unit (ICU) stay and hospital length of stay (LOS), and the proportion of bioprosthetic versus mechanical valves used.

STATISTICAL ANALYSIS. Baseline demographics and procedural, in-hospital, and post-discharge outcomes at the time of index TAVR were assessed and compared between those who underwent explantation and those who did not. Continuous variables were tested for distribution, were compared using analysis of variance for normally distributed variables or Kruskal-Wallis 1-way analysis of variance for non-normally distributed variables, and are presented as mean ± SD or median (interquartile range [IQR]), as appropriate. Binary variables are presented as number and percentage and were compared using chi-square tests or Fisher exact test, depending on cell sizes. We also assessed temporal trends in annual surgical explantation rates as well as proportions of surgical explants performed within 3 months, 6 months, and 1 year of index TAVR, based on the distribution of the time to surgical explant variable. Furthermore, we assessed the proportions of surgical explants according to different patient risk profiles as determined by Charlson scores. Charlson scores were calculated using the enhanced coding of Quan et al. (16) and modeled as restricted cubic splines into lower-risk (≤7), medium-risk (8–12), and higher-risk (>12) profiles.

Potential associations and risk factors for surgical explantation were examined by univariate analyses. Adjusted survival was evaluated with a backwards-conditional Cox proportional hazard model. Because there was evidence of a substantial effect of immortal time bias/survivor treatment selection bias in the explant group—which refers to a period of cohort follow-up time during which death could not occur because of exposure definition (i.e., surgical explantation)—a second time-dependent Cox proportional hazard model was developed using time to surgical explant as a time-dependent covariate. For patients who did not undergo explantation, a dummy value exceeding the longest interval was assigned (10,000 days), and a conditional variable was created where the event occurred if time in days (interval from index TAVR) < survival days. The Cox model was fitted after careful selection of baseline

FIGURE 1 Time to Surgical Explant and Corresponding Proportions



The median time to surgical explant was 212 days (interquartile range: 69 to 398 days). Of the 227 patients, the majority required surgical explantation within 1 year.

characteristics and peri-procedural variables based on clinical judgment, univariable assessment, and association with mortality. Correlations between variables were explored with the Pearson correlation coefficient, and highly correlated variables were not included in the multivariable model; if highly correlated variables were substantially associated with the outcomes of interest, the variable that best improved the predictive performance was included. The model included cardiac-specific variables that were roughly analogous to many Society of Thoracic Surgeons (STS)-predicted risk of mortality variables, as depicted in Supplemental Table 1. As a secondary analysis to account for the immortal time bias in our groupings, in addition to the time-dependent Cox proportional hazard regression analysis, we performed Kaplan-Meier analysis of survival using the landmark analysis approach with post-native TAVR window of 14 days as T0. This landmark time corresponded to the earliest time to surgical explant, which resulted in the exclusion of zero explant patients and 118 of the 132,633 native TAVR patients for the secondary analysis. All subjects had at least 22 months of survival follow-up available. We opted to use this approach to illustrate the survival differences between the explant and no-explant cohort instead of the Simon and Makuch modified Kaplan-Meier plots (17), because the landmark analysis method facilitates clinical interpretability of the study findings with the important caveat that conclusions are only generalizable to subjects who survived until the landmark time.

We examined whether there were temporal trends in 30-day, 90-day, and 1-year mortality after surgical explantation by the era of index TAVR procedure with a cut-off at December 2014, with early era to depict first-generation TAVR valves (2012 to 2014) and later era to depict second-generation TAVR valves (2015 to 2017), corresponding to their U.S. Food and Drug Administration approvals. Because STS-predicted risk scores cannot be calculated directly from CMS data, given its administrative nature, we performed additional analysis to further risk stratify patients into 2 subgroups. First, we used the implant year of index TAVR procedure with a cut-off of 2015 such that patients who underwent initial TAVR procedure prior to 2015 were considered the extreme/high-risk STS risk score cohort, whereas those undergoing initial TAVR procedure after 2015 also comprised of the high/intermediate STS risk score group. Second, we categorized our cohort into Charlson high-risk (scores >10) and low-risk (scores ≤10) patient profiles. These groupings were determined based on the distributions in our cohort and cut-offs associated with univariate analysis, and to further ensure that we had even groups of patients while preserving the mortality distributions of TAVR patients. Individual time-dependent Kaplan-Meier curves for overall survival

TABLE 1 Baseline Characteristics of Patients Undergoing Surgical Explantation of TAVR Valve (n = 227)

Age ≥85 yrs	24 (10.6)
Women	80 (35.2)
Dyslipidemia	164 (72.2)
Hypertension	189 (83.3)
Diabetes	121 (53.3)
PVD	29 (12.8)
Stroke or TIA	20 (8.8)
Anemia	147 (64.8)
COPD	79 (34.8)
Chronic kidney disease	138 (60.8)
Atrial fibrillation	71 (31.3)
Ischemic heart disease	172 (75.8)
AMI	15 (6.6)
Congestive heart failure	168 (74.0)
Previous PCI	27 (11.9)
Previous CABG surgery	55 (24.2)
Charlson score	11 (10-12)
Lower-risk profile (<8)	27 (11.9)
Medium-risk profile (8-12)	146 (64.3)
Higher-risk profile (>12)	54 (23.8)
Depression	49 (21.6)
Cancer	34 (15.0)

Values are n (%) or median (interquartile range). These characteristics are assessed at the time of surgical explantation procedure.

AMI = acute myocardial infarction; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; PCI = percutaneous coronary intervention; PVD = peripheral valvular disease; TAVR = transcatheter aortic valve replacement; TIA = transient ischemic attack.

TABLE 2 Procedural and In-Hospital Outcomes of Patients Undergoing Surgical Explantation of TAVR Valve (n = 227)

Time to surgical explant, days	212 (69-398)
Type of valve placed	
Mechanical	47 (20.7)
Bioprosthetic	180 (79.3)
Concomitant procedures	
Coronary artery bypass grafting	19 (8.4)
Other valve procedures	10 (4.4)
Etiology/indication	
Endocarditis	47 (20.7)
Bioprosthetic failure	180 (79.3)
In-hospital complications	
Bleeding complications	127 (55.9)
Transfusion with blood products	82 (36.1)
Permanent stroke	13 (5.7)
Acute kidney injury	66 (29.1)
Complete heart block	26 (11.5)
Length of stay, days	11 (8-16)
Intensive care unit stay, days	5 (1-10)
30-day mortality	30 (13.2)
90-day mortality	40 (17.6)
1-year mortality	52 (22.9)

Values are median (interquartile range) or n (%). These characteristics are assessed at the time and following the surgical explantation procedure.

TAVR = transcatheter aortic valve replacement.

were generated for each subgroup in the previous text, and an additional curve was generated that accounted for the interaction between the 2 subgroups. A 2-sided p value ≤0.01 was the criterion of significance. All analyses were conducted using SPSS version 23.0 (IBM, Armonk, New York) or R version 3.4.1 (R Foundation, Vienna, Austria). The study was reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology recommendations (Supplemental Appendix 1). Data analysis were performed between December 2019 and March 2020.

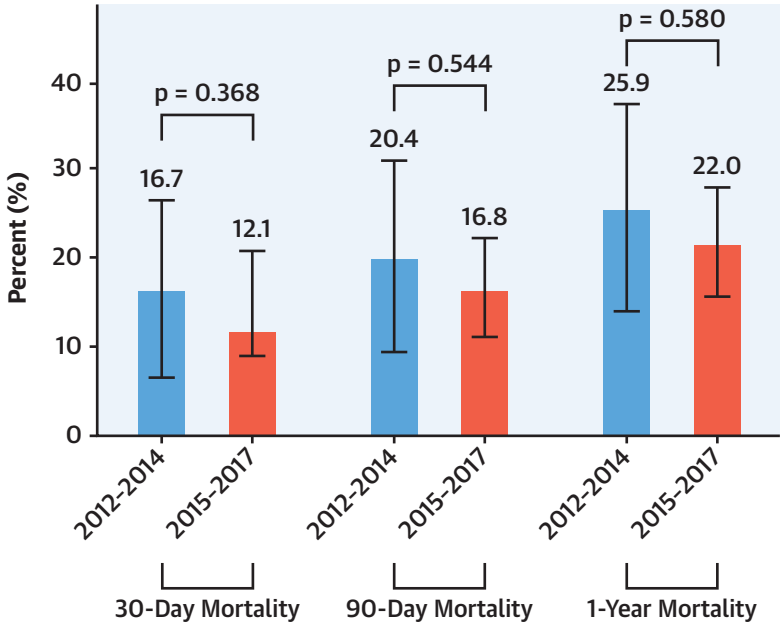
RESULTS

INCIDENCE AND TIMING OF SURGICAL EXPLANTATION. A total of 132,633 patients met study criteria, and surgical explantation was performed in 227 patients (0.2%) after the index TAVR. The incidence in the early TAVR era (pre-2015) was 0.28% (n = 90 per 32,724 patients), whereas it was 0.14% in the newer era (2015 and onward), which also included the intermediate-risk STS patients (n = 137 per 99,909 patients). The annual rate of surgical explantation varied from 0.09% to 1.7% with no time trend (p > 0.50). The median time to surgical explant was 212 days (IQR: 69 to 398 days). Of the 227 patients, 20 patients (8.8%) required surgical explantation within 30 days of discharge, 161 patients (70.9%) within 1 year, and 66 patients (29.1%) after 1 year (Figure 1).

BASELINE CHARACTERISTICS OF EXPLANT COHORT AT THE TIME OF SURGICAL EXPLANTATION. Distributions of baseline parameters are presented in Table 1. The mean age of the surgical explant cohort was 73.7 ± 8.9 years, and 35.2% were women. The prevalence of ischemic heart disease, diabetes, and CKD was 75.8%, 53.3%, and 60.8%, respectively. The median Charlson score was 11 (IQR: 10 to 12), and the majority of patients (64.3%) were classified as having a medium risk profile.

OPERATIVE CHARACTERISTICS AND POST-OPERATIVE OUTCOMES OF EXPLANT COHORT. The primary indication for reintervention was bioprosthetic failure (79.3%), and endocarditis accounted for 20.7% of the cases (Table 2). There were no detectable trends in the incidence of endocarditis (p > 0.05), although we were underpowered by our sample size. Furthermore, 29 patients (12.7%) underwent concomitant procedures, whereas a mechanical valve was placed in 20.7% of patients (Supplemental Table 2).

FIGURE 2 Time Sensitivity Analysis of Surgical Explant Outcomes by TAVR Era



The 30-day mortality during the early transcatheter aortic valve replacement (TAVR) era (2012 to 2014) was numerically higher (16.7% vs. 12.1%), although not statistically significant compared with the later TAVR era (2015 to 2017). The 90-day and 1-year mortality also did not differ substantially.

Overall, the 30-day and 1-year mortality rates were 13.2% and 22.9%, respectively. The rates of bleeding complications, permanent stroke, and AKI were 55.9%, 5.7%, and 29.1%, respectively at 30 days. The median ICU and hospital LOS were 5 days (IQR: 1 to 10 days) and 11 days (IQR: 8 to 16 days), respectively. When examining outcomes by the TAVR era, the 30-day mortality during the early TAVR era (2012 to 2014) was numerically higher (16.7% vs. 12.1%), although not statistically significant compared with the later TAVR era (2015 to 2017; $p = 0.37$). The 90-day and 1-year mortality also did not differ substantially (Figure 2). Additionally, the 30-day mortality rates did not vary by time to surgical explant ($p = 0.79$), and were not significantly different between the endocarditis and non-endocarditis patients (12.8% vs. 13.3%; $p = 1.00$), although the former group had a longer hospital LOS (15 days vs. 7 days; $p < 0.01$).

COMPARISON OF EXPLANT VERSUS NO-EXPLANT COHORT CHARACTERISTICS AND OUTCOMES AT THE TIME OF INDEX TAVR. Compared with the no-explant cohort, the explant cohort was significantly younger (mean age: 73.7 years vs. 81.7 years), and less likely to be female (35.2% vs. 47%; both $p < 0.001$). In terms of risk profile based on Charlson scores, the explant cohort was more likely a lower-risk profile cohort (15% vs. 2.4%) with a lower prevalence of HF (55.9% vs. 65.8%) but a high prevalence of diabetes (52% vs. 44.5%; all $p < 0.05$) (Table 3). Other baseline characteristics were not statistically significant between these 2 groups. There were also no statistical differences in the rates of bleeding complications, post-operative AKI, permanent stroke, ICU, and hospital LOS between the 2 groups (all $p > 0.05$).

FACTORS ASSOCIATED WITH SURGICAL EXPLANTATION. On univariate analysis, patients who underwent surgical explantation during the observation time were more likely to have diabetes (odds ratio [OR]: 1.35; 95% confidence interval [CI]: 1.04 to 1.76) and Charlson scores of 10 or under (OR: 2.31; 95% CI: 1.74 to 3.07) than those without surgical explantation (Supplemental Table 3). Multivariable analysis did not result in a predictive model, likely due to the very low prevalence of explantation in the group as a whole.

OVERALL SURVIVAL AND POST-EXPLANT SURVIVAL. The median duration of follow-up for survival was 22 months (IQR: 14 to 144 months). To compare the overall survival between the explant and no-explant cohort, we used a time-dependent Cox proportional hazard model to account for the immortal time bias—the period of cohort follow-up time during which

TABLE 3 Comparison of Baseline Characteristics and Procedural Outcomes of All TAVR Patients Stratified by Those Who Eventually Required Surgical Explantation of TAVR Valve Versus Those Who Did Not Require Any Reintervention

	Patients Requiring Surgical Explantation (n = 227)	Patients Not Requiring Reintervention (n = 132,406)	p Value
Characteristics			
Age, yrs	73.7 ± 8.9	81.7 ± 8.1	0.001
Age ≥85 yrs	18 (7.9)	55,693 (42.1)	0.001
Women	80 (35.2)	62,181 (47.0)	0.001
Dyslipidemia	156 (68.7)	91,153 (68.9)	0.947
Hypertension	186 (81.9)	110,211 (83.3)	0.598
Diabetes	118 (52.0)	58,806 (44.5)	0.023
PVD	29 (12.8)	17,897 (13.5)	0.837
Stroke or TIA	14 (6.2)	10,998 (8.3)	0.332
Anemia	114 (50.2)	67,780 (51.2)	0.791
COPD	69 (30.4)	34,323 (25.9)	0.128
Chronic kidney disease	100 (44.1)	63,901 (48.3)	0.207
Atrial fibrillation	52 (22.9)	35,627 (26.9)	0.137
Ischemic heart disease	159 (70.0)	99,740 (75.4)	0.062
Congestive heart failure	127 (55.9)	87,059 (65.8)	0.002
Previous PCI	27 (11.9)	11,092 (8.4)	0.066
Previous CABG surgery	55 (24.2)	27,650 (20.9)	0.220
Charlson score	10 (9–12)	11 (10–12)	0.001
Lower-risk profile (<8)	34 (15.0)	3,149 (2.4)	
Medium-risk profile (8–12)	159 (70.0)	102,548 (77.5)	
Higher-risk profile (>12)	34 (15.0)	26,591 (20.1)	
Depression	36 (15.9)	21,072 (15.9)	0.992
In-hospital complications			
Bleeding complications	48 (21.1)	28,424 (21.5)	0.994
Transfusion with blood products	30 (13.2)	14,843 (11.2)	0.345
Acute kidney injury	19 (8.4)	11,028 (8.3)	1.000
Complete heart block	30 (13.2)	12,535 (9.5)	0.063
Length of stay, days	4 (2–7)	4 (2–7)	0.088
Intensive care unit stay, days	1 (0–3)	1 (0–3)	0.611

Values are mean ± SD, n (%), or median (interquartile range). These characteristics are assessed at the time of index (initial) TAVR procedure.

Abbreviations as in Table 1.

death event could not occur in the explant group because the explant cohort had to have survived during this period to undergo surgical explantation. Failure to account for this delay period would have resulted in a spurious survival advantage (protective association) in favor of surgical explantation. After adjustment, surgical explantation was associated with a significantly higher mortality risk (hazard ratio [HR]: 4.03; 95% CI: 1.81 to 8.98) (Table 4). In our secondary analysis using the landmark analysis approach, actuarial Kaplan-Meier estimates of survival were significantly lower at 6 months (91.2% [95% CI: 87.5% to 92.9%] vs. 92.4% [95% CI: 92.3% to 94.6%]) and at 1 year (84.1% [95% CI: 79.4% to 85.9%] vs. 86.8% [95% CI: 86.6% to 88.4%]) for the explant cohort versus the no-explant ($p < 0.001$) (Figure 3).

SUBGROUP ANALYSIS. Within the explant cohort, we further evaluated whether very early explantation (≤6 months vs. >6 months) was associated with worsened post-explant outcomes. On univariate analysis, patients undergoing very early explantation did not differ from patients undergoing later explantation based on distributions of age, demographics, or cardiac risk factors (all $p > 0.25$). Cox proportional hazard modeling showed that the time to surgical explant was not associated with significant differences in survival (HR: 0.86; 95% CI: 0.48 to 1.52, for very early explantation) (Supplemental Figure 2). Likewise, the etiology (i.e., endocarditis), HF, or year of explant were all noncontributory (all $p > 0.05$), but CKD was the only significant risk factor (HR: 2.02; 95% CI: 1.11 to 3.68).

Additionally, we found no significant differences in 30-day, 90-day, or 1-year mortality when stratifying the explant cohort by TAVR implant year (i.e., extreme/high STS risk vs. high/intermediate STS risk) or Charlson high-risk versus low-risk patient profiles (Supplemental Table 4). Likewise, there were no differences in cumulative survival when stratifying the explant cohort by TAVR implant year, Charlson scores, or the interaction between the 2 (all $p > 0.05$) (Supplemental Figure 3).

DISCUSSION

This large, comprehensive, contemporaneous, and nationally representative analysis is the largest series to date that directly examines the incidence, timing, characteristics, and outcomes after surgical explantation of a TAVR valve. There were several key findings. First, the overall incidence of surgical explantation was low, but with a predilection toward younger patients with fewer comorbidities. Second, we found that most explants occurred within 1 year of index TAVR procedure, primarily due to bioprosthetic failure. Third, although 30-day mortality was high, it did not vary by the time to surgical explant, by TAVR era, or between the endocarditis and nonendocarditis patients. Finally, surgical explantation was associated with a significantly higher mortality risk after the index TAVR procedure (**Central Illustration**). However, within the explant cohort, etiology (i.e., endocarditis), the time-to-surgical explant, or year of explant were not associated with worse post-explant survival. Likewise, there were no survival differences within the explant cohort when stratified according to the different patient risk profiles. Although long-term data are warranted, these findings may help inform discussions regarding lifetime management of aortic stenosis, particularly in younger patients whose life expectancy will exceed that of valve durability.

The existing published data on surgical explantation after TAVR is scarce, and is only limited to few case reports and/or small single-center case series (8-10). For instance, Fukuhara et al. (8) recently reviewed their single-center TAVR experience of 1,442 patients and reported an acute device explantation incidence of 1% (n = 15). Their mean age was 73 years, with an STS-predicted risk of mortality score of 3.5% at the time of the index TAVR. Their overall in-hospital mortality rate following surgical explantation was 11.8%. Our study findings in terms of age, risk profile, and 30-day mortality corroborate their findings, albeit with a much larger, nationally representative, real-world sample. Furthermore, this present study includes a time period when TAVR was performed in either high- or extreme-risk patients, who may not have been considered for TAVR explant. This cherry-picking bias is the likely explanation for the younger and lower-risk patient profile in this series. Despite this patient selection bias, the in-hospital mortality was substantially high, and was almost 2-fold higher than those observed after reoperative surgical aortic valve replacement (SAVR) (18,19).

For most patients who require valve reintervention after their initial TAVR, TAVR-in-TAVR may be a treatment option provided the anatomy is favorable (13,14). However, there will be a subset of patients in whom surgical explantation may be warranted. Despite the very high mortality of infective endocarditis after TAVR, those with abscess, aneurysm, vegetations, uncontrolled infection, and heart failure will require surgical explantation of the TAVR valve (20,21). Additionally, in anatomic contraindications, such as a high risk of coronary obstruction with TAVR-in-TAVR (22-24) or clinically significant residual PVL, advanced transcatheter techniques, such as the use of the BASILICA leaflet laceration procedure (25) or percutaneous PVL closure with vascular plugs (26), may be performed. However, if these advance procedures cannot be performed, surgical explantation will be necessary. Additionally, surgical explantation may be needed in patients who prefer a mechanical prosthesis due to their age, ongoing need for anticoagulation, or patient preference. Our study showed that the majority of cases were SVD; however, we suspect that the causes of TAVR explant will include a spectrum of different etiologies, which including PVL and valve thrombosis in addition to SVD. We suspect that in these patients, multimodality imaging (e.g., transesophageal echocardiography, cardiac computed tomography) and anatomic evaluation will play a greater role in guiding clinical decision making, as our understanding of TAVR valve failures evolves.

TABLE 4 Multivariable Time-Dependent Cox Regression Analysis of All-Cause Mortality of All Patients Undergoing Index TAVR Procedure

		95% CI		
	HR	Lower	Upper	p Value
Surgical explantation	4.031	1.810	8.978	0.001
Metastatic cancer	2.410	1.866	3.114	0.001
Liver disease with complications	2.022	1.580	2.586	0.001
Chronic kidney disease	1.472	1.415	1.531	0.001
COPD	1.443	1.385	1.504	0.001
HF	1.343	1.277	1.413	0.001
Bicuspid AV	1.320	1.010	1.727	0.042
Ischemic heart disease	1.312	1.242	1.386	0.001
Male	1.174	1.130	1.219	0.001
DM	1.156	1.113	1.201	0.001
Sternotomy prior to index procedure	1.117	1.068	1.169	0.001
PVD	1.115	1.059	1.174	0.001
Age (per yr >75 yrs)	1.014	1.012	1.017	0.001
Time-dependent covariate	3.641	1.592	8.328	0.002

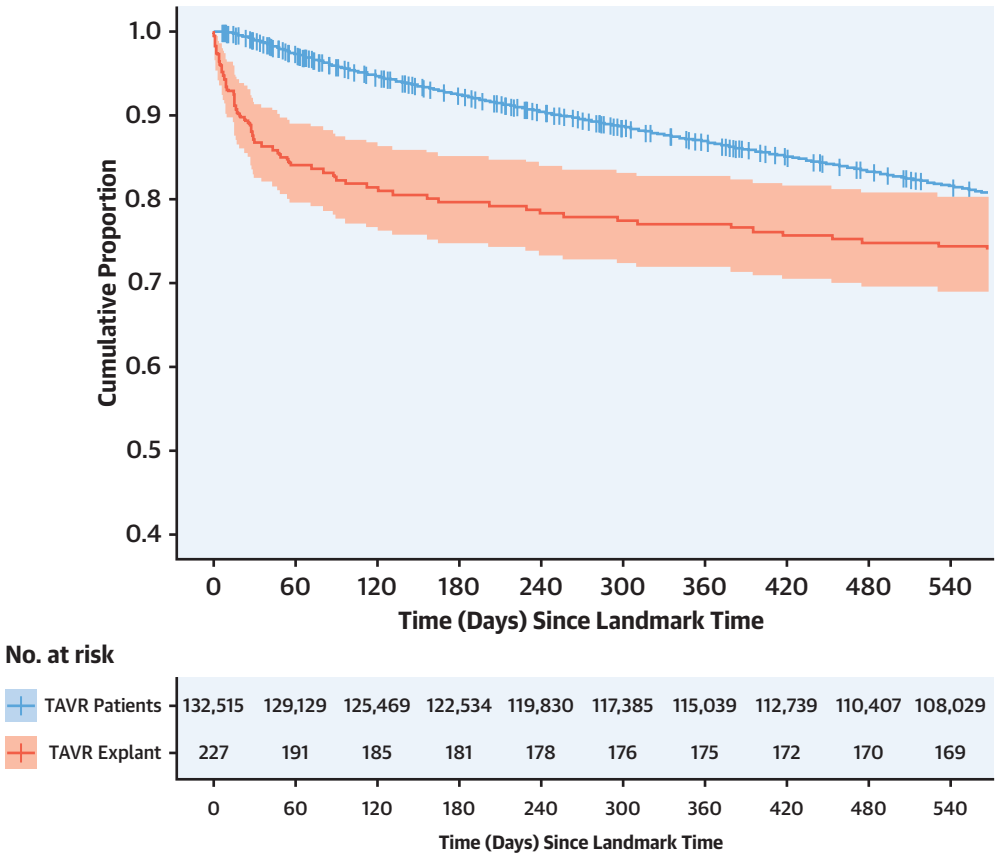
Noncontributory variables include: ischemic heart disease, coronary artery disease, Charlson risk score (spline or continuous), cerebrovascular disease, atrial fibrillation, etiology (endocarditis), and year of explant. Charlson <10 includes all low-risk and some medium-risk patients.

AV = aortic valve; CI = confidence interval; DM = diabetes mellitus; HF = heart failure; HR = hazard ratio; OR = odds ratio; other abbreviations as in Table 1.

The strengths of this timely study are 3-fold. First, it provides a comprehensive overview on the timing and etiology of surgical explantation after TAVR. By using the longitudinal design of the CMS data, we were able to link the index TAVR to the subsequent surgical explantation and account for the immortal time bias. Failure to account for this bias in analysis would have resulted in a spurious survival advantage in favor of surgical explantation. This will be the limitation of almost all other existing databases, such as the STS Adult Cardiac Surgery Database, the National Inpatient Sample, and the National Readmissions Database. Although an analysis of the STS database would help isolate the cohort who underwent surgical explantation, due to difficulty in linking the data to the American College of Cardiology/STS Transcatheter Valve Therapy Registry, there will be no reporting of the time-to-surgical-explant. The second advantage of the CMS database is the ability to obtain longitudinal outcomes beyond 30 days. This is not possible with the STS, as outcomes are limited to 30 days, and furthermore, other administrative databases (e.g., National Inpatient Sample) are only limited to in-hospital events. Finally, single-center and multicenter studies are not nationally representative and/or are limited by their small sample sizes, which limits the generalizability of findings.

Our findings provide some hypothesis-generation questions, particularly with respect to the lifetime management of aortic valve disease in younger, low-risk patients. In bioprosthetic SAVR, SVD typically

FIGURE 3 Kaplan-Meier Analysis of Survival Using the Landmark Analysis Approach to Account for the Immortal Time Bias

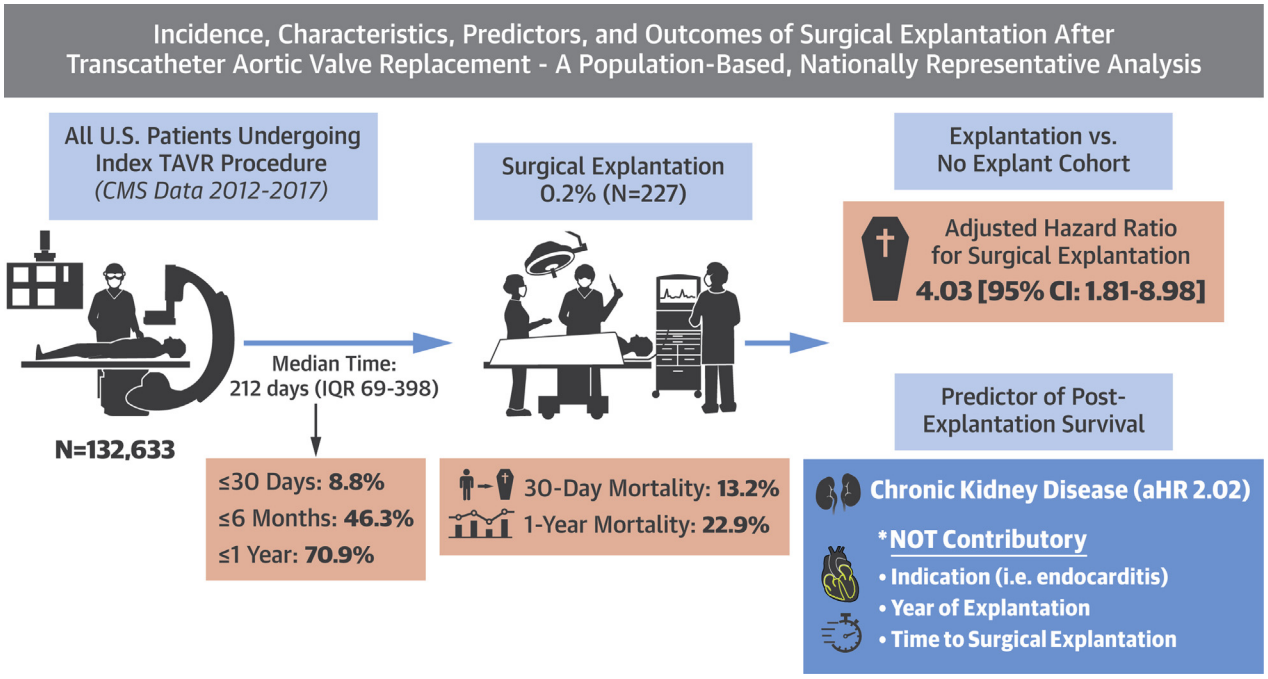


The post-native transcatheter aortic valve replacement (TAVR) window of 14 days was landmark time (T0) and corresponded to the earliest time-to-surgical-explant. The numbers at risk are 227 explant patients and 132,515 native TAVR patients (after excluding 118 patients who did not survive until the landmark time). All subjects had at least 22 months of survival follow-up available. Actuarial Kaplan-Meier estimates of survival were significantly lower at 6 months and at 1 year for the explant cohort versus the no-explant cohort ($p < 0.001$).

occurs starting around 10 to 12 years based on long-term data, even in younger patients (27,28). In our study, bioprosthetic failure was the reason for explant in 80% of patients, but our follow-up period falls short of the expected timeframe when bioprosthetic valves deteriorate. Although TAVR valves have shown promising data of low SVD up to 6 years from various clinical trials (29-31) and up to 10 years in isolated series (32,33), implantation of a TAVR valve in younger, low-risk patients would most certainly result in SVD during their lifetime and require reintervention. Additionally, initial TAVR-in-TAVR outcomes also appear to be promising, as demonstrated in a recent multicenter series of 212 redo-TAVR procedures, which showed satisfactory 30-day and 1-year survival outcomes (34). Although our mechanistic understanding of TAVR procedures in younger patients is still in its nascent stages, our study, together with the recent TAVR-in-TAVR, adds to the armamentarium of information that will serve as useful clinical benchmarks for the multifaceted and multidisciplinary heart teams as they seek to systematically and synergistically tailor the lifetime management of aortic valve disease.

STUDY LIMITATIONS. First, the CMS database is a hospital claims database and is subject to the shortcomings of other administrative datasets. Inconsistencies related to coding may overestimate or underestimate our findings although the ability of CMS data to track longitudinal encounters in TAVR patients allowed us to accurately capture subsequent SAVR procedures. Despite the strengths of the CMS database, as outlined in the previous text, it precludes a detailed assessment of patient

CENTRAL ILLUSTRATION **Summary of Key Findings of This Study**



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Surgical explantation was performed in 227 patients (0.2%) after the index transcatheter aortic valve replacement (TAVR). The incidence in the early TAVR era (pre-2015) was 0.28%, whereas it was 0.14% in the newer era (2015 and onward), which also included the intermediate-risk Society of Thoracic Surgeons patients. The median time to surgical explant was 212 days (interquartile range: 69 to 398 days). Of the 227 patients, 20 patients (8.8%) required surgical explantation within 30 days of discharge, 161 patients (70.9%) within 1 year, and 66 patients (29.1%) after 1 year.

presentation, procedural and echocardiographic details, STS risk scores, and granular details on endocarditis patients. Given CMS restrictions on cell size reporting of <10, we were unable to report details of certain variables. Specifically, we were interested in the patient group that required aortic root replacement; however, this was not reportable due to small numbers. The floor effects of our sample size precluded meaningful analysis of annual trends as well as instantaneous hazard densities. We were unable to determine the exact causes of bioprosthesis failure or differentiate between the TAVR valve type utilized (e.g., balloon-expandable vs. self-expanding), or to account for the surgeon selection bias for explant or preference for mechanical versus bioprosthetic valve. We anticipate that the ongoing EXPLANT-TAVR (surgical EXPLANTation After Transcatheter Aortic Valve Replacement [TAVR] Failure: An International Registry), a retrospective and prospective international registry on TAVR explant, will help us better understand detailed mechanisms of explant and modes of surgical intervention (Supplemental Appendix 2).

CONCLUSIONS

The present study provides updated evidence on the incidence, timing, and outcomes of surgical explantation of a TAVR prosthesis. Although the overall incidence was low, short-term mortality was high. These findings stress the importance of future mechanistic studies on TAVR explantation and may have implications on lifetime management of aortic stenosis, particularly in younger patients.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The need for surgical explantation of prosthetic aortic valves deployed by catheter techniques (TAVR) is low, but 30-day and 1-year mortality rates are high.

TRANSLATIONAL OUTLOOK: Long-term follow-up of larger cohorts is warranted to clarify the implications of these observations for patients with aortic stenosis whose life expectancy exceeds the anticipated durability of valve prostheses after TAVR.

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KEY WORDS surgical aortic valve replacement, TAVR explantation, transcatheter aortic valve replacement

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