Survival and long-term outcomes after mitral valve replacement in patients aged 18 to 50 years

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ABSTRACT

Objective: To provide long-term data on survival and major morbidity after mitral valve replacement in patients aged 18 to 50 years.

Methods: Retrospective analysis of 2727 patients aged 18 to 50 years who underwent isolated mitral replacement in California and New York from 1997 to 2006. Median follow-up time was 12.4 years (maximum 15.0 years). The primary endpoint was mortality; secondary endpoints were stroke, major bleeding, and reoperation. Propensity matching yielded 373 patient pairs.

Results: Bioprosthetic valve use increased from 10% to 34% between 1997 and 2014 ($P < .001$). Among propensity score-matched patients, actuarial 15-year survival was 74.3% (95% confidence interval [CI], 69.0%-78.7%) after bioprosthetic versus 80.8% (95% CI, 75.1%-85.3%) mechanical valve replacement (hazard ratio [HR], 1.67; 95% CI, 1.21-2.32, $P = .002$). At 15 years after mitral valve replacement, the cumulative incidence of stroke was similar (9.1% [95% CI, 6.0%-13.0%] vs 9.7% [95% CI, 6.7-13.4]; HR, 0.95 [95% CI, 0.57-1.59]); the cumulative incidence of major bleeding events was similar (7.9% [95% CI, 5.0%-11.5%] vs 11.5% [95% CI, 7.6%-16.2%]; HR, 0.78 [95% CI, 0.46-1.32]); and the cumulative incidence of reoperation after bioprosthetic valve replacement was greater (19.9% [95% CI, 15.4%-24.8%] vs 5.7% [95% CI, 3.5%-8.7%]; HR, 20.3 [95% CI, 4.0-102.8]), respectively.

Conclusions: The significant survival benefit associated with mechanical mitral valve replacement in adults ≤ 50 years may be due to the practice of implanting bioprostheses in sicker patients or those judged less likely to comply with long-term medication despite adjustment for baseline characteristics in propensity score matching. (J Thorac Cardiovasc Surg 2018;155:96-102)

Survival in propensity-matched adults aged ≤ 50 years according to mitral prosthesis type.

Central Message

In patients aged 18 to 50 years, bioprosthetic mitral valve replacements are used increasingly often but are associated with lower survival at 15 years compared with mechanical valves.

Perspective

Bioprosthetic mitral valve use has increased in patients aged 18 to 50 years despite few supporting data. We observed worse survival and freedom from reoperation, without a benefit in freedom from stroke or bleeding, compared with mechanical valves. This may reflect differences in bioprosthesis durability or patient characteristics and should be taken into account during preoperative decision-making.

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Approximately 10% of patients undergoing mitral valve replacement in the United States are adults < 50 years of age.¹ Current consensus guidelines favor mechanical over bioprosthetic valve replacement in this age group because the risks of structural valve degeneration and reoperation

associated with bioprostheses are thought to outweigh the increased risk of hemorrhagic and embolic events associated with mechanical valves and life-long anticoagulation.^{2,3} These recommendations are based primarily on the results of 2 randomized controlled trials that found no significant difference in late survival⁴⁻⁶ but that were performed during the 1970s and 1980s in older patients who predominantly underwent aortic rather than mitral valve replacement and on more recent,

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Abbreviations and Acronyms

CI	= confidence interval
HR	= hazard ratio
ICD-9-CM	= <i>International Classification of Diseases, 9th Revision, Clinical Modification</i>

underpowered single-center retrospective series.⁷⁻¹² We therefore analyzed a cohort of patients ≤ 50 years of age drawn from 2 states and 171 hospitals to quantify long-term mortality, stroke, reoperation, and bleeding after mitral valve replacement according to prosthesis type, in a broad cross-section of contemporary clinical practice.

METHODS

Study Design

We identified all patients aged 18 to 50 years undergoing primary mitral valve replacement in California and New York State between January 1, 1997, and December 31, 2006. Patients were identified from 2 mandatory all-payer administrative databases: The Office of Statewide Health Planning and Development in California State and the Statewide Planning and Research Cooperative System. Both databases capture individual patient data on every hospital discharge, ambulatory surgical procedure, and emergency department visits in each state.

Exclusion criteria consisted of out-of-state residency, previous valve replacement or repair, previous heart transplantation, concomitant valve replacement or repair of any other valve, congenital cardiac history or procedures, endocarditis, and concomitant coronary artery bypass grafting (Table E1).

The *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) procedure codes 35.23 and 35.24 were used to identify bioprosthetic and mechanical mitral replacements, respectively. The ICD-9-CM diagnosis codes from the index hospitalization, and all hospitalizations up to 2 years before the index hospitalization, were used to determine patient comorbid conditions at baseline (Table E2). The Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai, the Committee for the Protection of Human Subjects of California State, and the New York State Department of Health data protection review board approved this study with a waiver of informed consent.

Study Endpoints

All-cause mortality was the primary outcome, and the secondary outcomes were stroke, major bleeding, and mitral valve reoperation. Deaths were captured from California and New York State Vital Death Records via their respective Departments of Health. Additional death records were collected from the discharge disposition from any subsequent inpatient, emergency department, or ambulatory surgery visits, as well as from the Social Security Death Master File. Stroke during the index admission was defined as a postoperative cerebrovascular accident and in subsequent admissions as a primary diagnosis of ischemic or hemorrhagic cerebrovascular event. Transient ischemic attacks were excluded from this definition. Major bleeding was defined as a primary diagnosis of any bleeding event that required admission to hospital. Reoperation was defined as mitral valve replacement in subsequent admissions. ICD-9-CM codes were used to identify these late events (Tables E3 and E4). Patients free from death, stroke, major bleeding, or reoperation were censored on December 31, 2014.

Statistical Analysis

Means with standard deviations are used to report continuous variables, and proportions are used to report categorical variables. The Student *t* test

for normally distributed continuous variables and Pearson χ^2 test for categorical variables as well as standardized differences for both continuous and categorical variables were used to quantify the differences in baseline characteristics between patients receiving bioprosthetic and mechanical prosthetic mitral valves. The Kolmogorov test was used to determine normality in continuous variables. Non-normal continuous variables are reported as median with interquartile ranges, and differences were tested via the Wilcoxon-Mann-Whitney test. Trend analysis was performed with the Cochran-Armitage test on patients receiving mitral valve replacements between January 1, 1997, and December 31, 2014.

To eliminate confounding due to intrinsic differences in baseline characteristics between the bioprosthetic and mechanical valve replacement cohorts, propensity score matching was performed. Propensity scores were calculated with a logistic regression with bioprosthetic valve implantation as the outcome and all patient baseline characteristics (admission urgency, index surgery year, age, sex, race, coagulation defects, hypertension, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, congestive heart failure, atrial fibrillation, chronic obstructive pulmonary disease, chronic kidney disease, liver disease, cancer) included in the model as covariates.^{13,14} The area under the receiver operating characteristic curve for the model was 0.78. Patients were then matched 1:1 using a caliper of 0.01 of the logit of the propensity score. Differences in baseline characteristics and 30-day complication incidence between patients in both groups were detected with the use of the paired *t* test for normally distributed continuous variables, the Wilcoxon signed rank sum test for non-normally distributed continuous variables, and the McNemar test for categorical variables; standardized differences were also reported.

Survival curves of the primary outcome of mortality were constructed with the Kaplan-Meier method; prostheses were compared with a marginal Cox model with a robust sandwich variance estimator.

Competing risk analysis of the secondary outcomes—stroke, major bleeding, and reoperation—was performed by creating cumulative incidence functions. For each end point, adjusted hazard ratios were calculated with Cox proportional hazards models. The proportional hazards assumption was assessed in each model and found to be intact except reoperation and, if violated, the hazard ratios at different follow-up time points were reported.

To assess the robustness of the findings, all analyses were repeated in the full patient cohort as a sensitivity analysis using multivariable analysis with marginal Cox models with robust sandwich variance estimators controlling for admission urgency, index surgery year, age, sex, race, coagulation defects, hypertension, diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease, congestive heart failure, atrial fibrillation, chronic obstructive pulmonary disease, chronic kidney disease, liver disease, cancer, and clustering of patients within hospitals. All these sensitivity analyses confirmed the main findings and were included in the supplementary documents (Table E5).

All statistical tests were 2-tailed and an alpha level of 0.05 considered statistically significant. Statistical analyses were carried out with SAS version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Study Population

We identified 5818 patients aged 18 to 50 years who underwent mitral valve replacement. After excluding patients from out-of-state (4.9%, *n* = 282) and with previous valve replacement or repair (6.8%, *n* = 398), previous heart transplant (<0.3%, *n* < 15), concomitant valve replacement or repair (26.1%, *n* = 1520), congenital cardiac history or procedure (2.5%, *n* = 145), endocarditis (18.8%, *n* = 1095), and concomitant coronary artery bypass grafting (9.4%, *n* = 544), the study cohort

TABLE 1. Patient baseline characteristics after propensity score matching, by type of prosthesis

Baseline characteristics	Bioprosthetic (N = 373)	Mechanical (N = 373)	Standardized difference, %	P value
Demographics				
Age, median [IQR], y	42 [36-47]	42 [36-47]	10.8	.12
18-30	57 (15.3)	49 (13.1)		.68
31-40	105 (28.2)	98 (26.3)		
41-50	211 (56.6)	226 (60.6)		
Men	134 (35.9)	140 (37.5)	3.3	.64
New York State resident	227 (60.9)	211 (56.6)	8.7	.23
Race				
White (non-Hispanic)	180 (48.3)	183 (49.1)	1.6	.99
African-American (non-Hispanic)	72 (19.3)	71 (19.0)	0.7	
Other	121 (32.4)	119 (31.9)	1.2	
Emergent/urgent admission	162 (43.4)	144 (38.6)	9.8	.15
Comorbidities				
Coagulation/platelet disorders	20 (5.4)	20 (5.4)	0.0	1.00
Hypertension	100 (26.8)	103 (27.6)	1.8	.81
Diabetes mellitus	26 (7.0)	28 (7.5)	2.1	.78
Coronary artery disease	74 (19.8)	66 (17.7)	5.5	.46
Peripheral vascular disease	6 (1.6)	5 (1.3)	2.2	.76
Cerebrovascular disease	37 (9.9)	29 (7.8)	7.6	.29
Congestive heart failure	189 (50.7)	191 (51.2)	1.1	.88
Atrial fibrillation	77 (20.6)	94 (25.2)	10.9	.12
Chronic obstructive pulmonary disease	76 (20.4)	69 (18.5)	4.7	.49
Chronic kidney disease	23 (6.2)	26 (7.0)	3.3	.66
Dialysis dependent	17 (4.6)	17 (4.6)	0.0	1.00
Liver disease	15 (4.0)	22 (5.9)	8.7	.25
Cancer	15 (4.0)	10 (2.7)	7.5	.30
Year of surgery				
1997	24 (6.4)	35 (9.4)	10.9	.22
1998	23 (6.2)	22 (5.9)	1.1	
1999	33 (8.8)	27 (7.2)	5.9	
2000	29 (7.8)	39 (10.5)	9.3	
2001	34 (9.1)	40 (10.7)	5.4	
2002	48 (12.9)	35 (9.4)	11.1	
2003	43 (11.5)	28 (7.5)	13.7	
2004	48 (12.9)	55 (14.7)	5.4	
2005	42 (11.3)	60 (16.1)	14.1	
2006	49 (13.1)	32 (8.6)	14.7	

IQR, Interquartile range.

comprised 2727 patients who underwent either bioprosthetic (14.0%, n = 382) or mechanical (86.0%, n = 2345) mitral valve replacement. Propensity score matching yielded 373 patient pairs. The maximum follow-up time was 15.0 years (median 12.4 years).

Patient Characteristics

Use of bioprosthetic mitral replacements increased from 10.1% in 1997 to 33.6% in 2014 ($P < .001$; Figure E1). Patients who received bioprosthetic valves had a greater prevalence of emergent/urgent admission (39.0% vs 26.6%, $P < .001$) but a lower prevalence of atrial fibrillation (24.6% vs 34.8%, $P < .001$) (Table E6). In the propensity score-matched groups, there were no significant differences

in patient characteristics (Table 1) or 30-day outcomes after bioprosthetic versus mechanical valve replacement, suggesting that these groups were well matched (Table 2).

Survival

We observed a significant difference in long-term survival between bioprosthetic and mechanical mitral valves in the propensity score-matched groups (Figure 1). Actuarial 5-, 10-, and 15-year survival were 86.1% (95% confidence interval [CI], 82.1%-89.2%), 79.1% (95% CI, 74.6%-83.0%), and 74.3% (95% CI, 69.0%-78.7%) in the bioprosthetic group compared with 94.1% (95% CI, 91.2%-96.1%), 88.8% (95% CI, 85.1%-91.6%), and 80.8% (95% CI, 75.1%-85.3%) in the mechanical group

TABLE 2. Thirty-day outcomes after mitral valve replacement in propensity score-matched patients, by type of prosthesis

Patient cohort	Outcome	Prosthesis type, n (%)		P value
		Bioprosthetic (n = 373)	Mechanical (n = 373)	
Propensity score-matched patients	Mortality	10 (2.7)	3 (0.8)	.05
	Stroke	3 (0.8)	4 (1.1)	.71
	Atrial fibrillation	54 (14.5)	52 (13.9)	.84
	Acute kidney injury	15 (4.0)	11 (3.0)	.41
	Respiratory failure	40 (10.7)	45 (12.1)	.56

(hazard ratio [HR], 1.67; 95% CI, 1.21-2.32, $P = .002$) in the propensity score-matched cohort, respectively. There was a similar survival benefit associated with mechanical valves in the overall cohort (HR, 1.39; 95% CI, 1.05-1.83, $P = .02$), respectively (Table E5). In analysis of each age group, no survival benefit was observed in mechanical valve between age 18 to 30 and 31 to 40 years, but patients who had mechanical valve had significantly better survival than patients with bioprosthetic valve between age 41 and 50 (Figure E2).

Stroke

There was no significant difference in the risk-adjusted cumulative incidence of stroke between bioprosthetic and mechanical mitral valves at 15 years in the propensity score-matched cohort. In the propensity score-matched cohort, the cumulative incidence of stroke at 5, 10, and 15 years was 4.8% (95% CI, 3.0%-7.3%), 7.1% (95% CI, 4.8%-10.0%), and 9.1% (95% CI, 6.0%-13.0%) in

patients who underwent bioprosthetic mitral valve replacement versus 5.4% (95% CI, 3.4%-8.0%), 8.9% (95% CI, 6.2%-12.1%), and 9.7% (95% CI, 6.7%-13.4%) in patients who underwent mechanical mitral valve replacement, respectively (HR, 0.95; 95% CI, 0.57-1.59) (Figure 2, A). The 30-day mortality after stroke was 5.3%. The results of the multivariable analysis of stroke in the full patient cohort are shown in Table E5.

Major Bleeding

There was no significant difference in the risk-adjusted cumulative incidence of major bleeding between bioprosthetic and mechanical valves at 15 years in the propensity score-matched cohort. The cumulative incidence of bleeding in the overall cohort at 5, 10, and 15 years was 4.3% (95% CI, 2.6%-6.7%), 5.9% (95% CI, 3.8%-8.6%), and 7.9% (95% CI, 5.0%-11.5%) in patients who underwent bioprosthetic mitral valve replacement versus 4.6% (95% CI, 2.8%-7.0%), 8.4% (95% CI,

FIGURE 1. Kaplan-Meier survival curves in propensity score-matched patients aged 18 to 50 years after mitral valve replacement. HR, Hazard ratio; CI, confidence interval.

FIGURE 2. Cumulative incidence of major morbidity in propensity score-matched patients aged 18 to 50 years after mitral valve replacement according to prosthesis type: A, stroke; B, major bleeding; and C, reoperation. HR, Hazard ratio; CI, confidence interval.

5.8%-11.6%), and 11.5% (95% CI, 7.6%-16.2%) in patients who underwent mechanical mitral valve replacement, respectively (HR, 0.78; 95% CI, 0.46-1.32) (Figure 2, B). The 30-day mortality after major bleeding was 6.8%. The results of the multivariate analysis of major bleeding in the full patient cohort are shown in Table E5.

Reoperation

Mechanical valves were associated with a significantly lower rate of mitral valve reoperation than bioprosthetic valves in the propensity score-matched cohort. The cumulative incidence of mitral valve reoperation in the propensity score-matched cohort at 5, 10, and 15 years in patients with bioprosthetic mitral valves was 4.6% (95% CI, 2.8%-7.0%), 14.1% (95% CI, 10.6%-18.0%), and 19.9% (95% CI, 15.4%-24.8%) versus 2.7% (95% CI, 1.4%-4.7%), 4.7% (95% CI, 2.8%-7.2%), and 5.7% (95% CI, 3.5%-8.7%) in patients with mechanical valves, respectively (adjusted HR at 15 years 20.3; 95% CI,

4.0-102.8) (Figure 2, C). An overall 30-day mortality after reoperation was 2.5%. The results of the multivariable analysis of reoperation in the full patient cohort are shown in Table E5.

DISCUSSION

This study provides long-term data on survival and major morbidity after mitral valve replacement in young adults from a broad cross-section of contemporary clinical practice. Our data show first that up to one third of patients aged ≤ 50 years undergoing mitral valve replacement receive bioprosthetic valves and second the much greater risk of reoperation does not appear to be offset by any reduction in stroke and major bleeding rates compared with mechanical valves. The poorer survival that we observed in patients who received bioprosthetic valves confirms the findings of much smaller retrospective studies.⁹⁻¹¹

Studies comparing bioprosthetic with mechanical mitral valve replacement in this age group previously have been

limited to single-center retrospective studies, with conflicting results regarding both the comparative risks of reoperation and survival. For example, Kaneko and colleagues¹⁰ reported better survival and freedom from reoperation at 15 years with mechanical mitral valve replacement over bioprosthetic in 125 propensity-matched patients pairs <65 years of age, whereas others have observed no significant differences in long-term survival.^{8,12} The comprehensive patient level data and large size of our cohort, which represents contemporary practice across 2 large states and 171 institutions, allowed us to adjust for key patient and provider characteristics, confirmed by the very similar 30-day outcomes in the mechanical and bioprosthetic propensity score-matched patient groups.

There are several potential explanations for our observation of a survival benefit with mechanical mitral valves. First, despite propensity matching, the likelihood remains that we are comparing substantially different patient populations. This is because of the established practice of implanting bioprosthetic valves in patients with reduced life expectancy or in patients judged unlikely to comply with life-long anticoagulation.^{2,3} Without patient-level data on these specific aspects of decision making, these important factors cannot be adjusted for retrospectively, potentially explaining why smaller retrospective studies show significantly worse survival in recipients of bioprosthetic valves.

The second potential reason for the reduced survival associated with bioprosthetic valves is the accelerated structural valve degeneration seen in the mitral position in younger patients.⁶ This means that young patients with bioprosthetic mitral valves bear an earlier burden of severe valvulopathy and reoperation which, in the absence of any survival benefits from reduced stroke and major bleeding events, may be an important determinant of their worse survival. In our propensity score-matched cohort, the cumulative incidence of reoperation was 19.9% in bioprosthetic patients versus 5.7% in mechanical patients. These results are well known: Kaneko and colleagues,¹⁰ Carrel and colleagues,⁷ and Ruel and colleagues¹⁵ all report high rates of structural valve degeneration and replacement among these younger patients. The implications of these data are greatest for patients unable or unwilling to comply with long-term anticoagulation. The commonest reasons for this in young patients are difficulty accessing health care and child-bearing, rather than comorbid contraindications to anticoagulation.¹⁶ These considerations are particularly relevant for patients from low- and middle-income countries where rheumatic valve disease is more prevalent in young women and long-term access to health care is less readily available.¹⁷ For many patients without reliable access to health care, and particularly those considering pregnancy, the immediate safety profile of bioprosthetic

valves outweighs the risks posed by accelerated structural degeneration. Although these bioprosthetic valves are accompanied by significantly high rates of reoperation, only the placement of a bioprosthetic valve will allow for a potential future valve-in-valve replacement. It would be difficult to counsel patients on the merits of a bioprosthetic valve in the hopes of a future valve-in-valve rescue, as this emerging technology's applicability and durability remain to be seen in younger, lower-risk patients.¹⁸

Limitations

Although this study represents a broad sample of contemporary practice in North America and provides valuable long-term outcome data, there are substantial limitations in how these data can be interpreted. This is primarily because, as described previously, selection bias cannot be adequately controlled for retrospectively in young patients undergoing mitral valve replacement without more information on the rationale for valve choice. Residual confounding may exist even after propensity score matching. Second, the data are abstracted from clinical records by administrative coders and provide limited information on the etiology, severity, and sequelae of valve disease and comorbidities and no data on the model or size of each valve prosthesis beyond whether it is mechanical or bioprosthetic. Third, the number of patients at risk at 15 years is relatively small. Fourth, we may have underestimated the rate of the secondary endpoints because identifying them depends on patients remaining within their state; nevertheless, we believe that this equally affects both groups and does not diminish the study's comparative value. Finally, the follow-up available to us does not fully represent the relative lifetime risks in this patient age group. Combining this with data from additional states or national clinical datasets may allow a more definitive analysis of outcomes in this patient population that is likely to remain underrepresented in clinical trials.

CONCLUSIONS

In adults ≤ 50 years who undergo mitral replacement, the much greater risk of reoperation with bioprosthetic valves is not mitigated by a reduction in stroke and major bleeding rates compared to mechanical valves. The significant survival benefit that we observed with mechanical mitral valve replacement may be due to accelerated structural degeneration in mitral bioprostheses. These findings should inform decision-making in patients, particularly those basing prosthesis selection on lifestyle choices rather than access to health care or contraindications to lifelong anticoagulation.

Conflicts of Interest Statement

Dr Chikwe received speaker honoraria from Edwards Lifesciences. The Icahn School of Medicine at Mount Sinai

receives royalty payments from Edwards Lifesciences and Medtronic for intellectual property related to Dr Adams' involvement in the development of 2 mitral valve repair rings and 1 tricuspid valve repair ring. Dr Adams is the National Co-Principal Investigator of the CoreValve United States Pivotal Trial, which is supported by Medtronic. None of the sponsoring organizations had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. All other authors have nothing to disclose with regard to commercial support.

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Key Words: mitral valve, mitral valve replacement, nonelderly patients, prosthetic valve choice, long-term outcomes

FIGURE E1. Trend in mechanical or bioprosthetic valve usage for mitral valve replacement in patients aged 18 to 50 years: *P* value for trend calculated by the Cochran-Armitage test was <.001.

FIGURE E2. Survival curves in propensity score-matched patients aged 18 to 50 years according to the prosthesis type stratified by age: A, 18 to 30 years; B, 31 to 40 years; C, 41 to 50 years. *HR*, Hazard ratio; *CI*, confidence interval.

TABLE E1. Definitions of exclusion criteria

Exclusion criterion	International Classification of Diseases, 9th Edition, Clinical Modification codes
Endocarditis	Diagnosis codes (from index and previous admission) 421, 4210, 4211, 4219, 11281, 03642, 09884, 11504, 11514, and 11594
Previous valve replacement	Diagnosis code (from index admission) V433 Procedure codes (from previous admissions) 3520, 3521, 3522, 3523, 3524, 3525, 3526, 3527, and 3528
Previous valve repair	Procedure codes (from previous admissions) 3510, 3511, 3512, 3513, 3514, and 3533
Previous heart transplant	Procedure codes (from index and previous admissions) 336, 3751 Diagnosis codes (from index and previous admissions) V421, 99683
Congenital cardiac disease	Diagnosis code (from index and previous admission) 7450, 7451, 74510, 74511, 74512, 74519, 7451, 7453, 7467, 7457, 7456, 74560, 74561, 74569, 7460, 74601, 74602, 74609, 7461, 7462, 7473, 7474, 74740, 74741, 74742, 74749, 7458, 7459, 7475, 7468, 74681, 74682, 74683, 74684, 74689, 7469, 7479, and V1365 Procedure codes (from previous admission) 354, 3541, 3542, 3553, 3554, 3562, 3563, 3573, 358, 3581, 3582, 3583, 3584, 359, 3591, 3592, 3593, 3594, 3595, 3598, 3599, 390, and 3921
Concomitant congenital cardiac surgery	Procedure codes (from index admission) 354, 3541, 3542, 3553, 3554, 3562, 3563, 3573, 358, 3581, 3582, 3583, 3584, 359, 3591, 3592, 3593, 3594, 3595, 3598, 3599, 390, and 3921
Concomitant valve replacement	Procedure codes (from index admission) 3520, 3521, 3522, 3525, 3526, 3527, and 3528
Concomitant coronary artery bypass graft surgery	Procedure codes (from index admission) 361, 3610, 3611, 3612, 3613, 3614, 3615, 3615, 3617, and 3618

TABLE E2. Definitions of baseline characteristics

Baseline characteristic	International Classification of Diseases, 9th Edition, Clinical Modification codes
Coagulation or platelet disorders	<i>Diagnosis codes (from index and previous admissions)</i> 286, 2861-2865, 28652, 28653, 28659, 2866, 2867, 2869, 287, 2870-2873, 28730, 28731, 28732, 28733, 28739, 2874, 2875, 2878, and 2879
Hypertension	<i>Diagnosis codes (from index and previous admissions)</i> 401, 4011, 4019, 402, 4020, 40200, 40201, 4021, 4029, 40290, 40291, 403, 4030, 40300, 40301, 4031, 40310, 40311, 4039, 40390, 40391, 404, 4040, 40400, 40401, 40402, 40403, 4041, 40410, 40411, 40412, 40413, 4049, 40490, 40491, 40492, 40493, 405, 4050, 40501, 40509, 4051, 40511, 40519, 4059, 40591, 40599, and 4372
Diabetes	<i>Diagnosis codes (from index and previous admissions)</i> 249, 2490, 24900, 24901, 2491, 24910, 24911, 2492, 24920, 24921, 2493, 24930, 24931, 2494, 24940, 24941, 2495, 24950, 24951, 2496, 24960, 24961, 2497, 24970, 24971, 2498, 24980, 24981, 2499, 24990, 24991, 250, 2500, 25000, 25001, 25002, 25003, 2501, 25010, 25011, 25012, 25013, 2502, 25020, 25021, 25022, 25023, 2503, 25030, 25031, 25032, 25033, 2504, 25040, 25041, 25042, 25043, 2505, 25050, 25051, 25052, 25053, 2506, 25060, 25061, 25062, 25063, 2507, 25070, 25071, 25072, 25073, 2508, 25080, 25081, 25082, 25083, 2509, 25090, 25091, 25092, and 25093
Coronary artery disease	Un-revascularized <i>Diagnosis codes (from index and previous admissions)</i> 410, 4100, 41000, 41001, 41002, 4101, 41010, 41011, 41012, 4012, 40120, 41021, 41022, 4103, 41030, 41031, 41032, 4104, 41040, 41041, 41042, 4105, 41050, 41051, 41052, 4106, 41060, 41061, 41062, 4107, 41070, 41071, 41072, 4108, 41080, 41081, 41082, 4109, 41090, 41091, 41092, 411, 4110, 4111, 4118, 41181, 41189, 412, 413, 4130, 4131, 4139, 414, 4140, 41400, 41401, 41402, 41403, 41404, 41405, 41406, 41407, 4142, 4143, 4144, 4295, 4296, 4297, 42971, and 42979 Previous percutaneous coronary intervention <i>Diagnosis codes (from index and previous admissions)</i> V4582 <i>Procedure codes (from previous admissions)</i> 0066, 1755, 3601, 3602, 3603, 3604, 3605, 3606, 3607, 3608, and 3609 Previous coronary artery bypass grafting <i>Diagnosis codes (from index and previous admissions)</i> V4581 <i>Procedure codes (from previous admissions)</i> 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, and 3619
Peripheral vascular disease	<i>Diagnosis codes (from index and previous admissions)</i> 4400, 4401, 4402, 44020, 44021, 44022, 44023, 44024, 44029, 4403, 44030, 44031, 44032, 4404, 4408, 4409, 4471, 9961, 99662, 99674, and V434
Cerebrovascular disease	<i>Diagnosis codes (from index and previous admissions)</i> 3623, 36230, 36231, 36232, 36233, 36234, 36235, 36236, 36237, 3466, 34660, 34661, 34662, 34663, 430, 431, 432, 4320, 4321, 4329, 433, 4330, 43300, 43301, 4331, 43310, 43311, 4332, 43320, 43321, 4333, 43330, 43331, 4338, 43380, 43381, 4339, 43390, 43391, 434, 4340, 43400, 43401, 4341, 43410, 43411, 4349, 43490, 43491, 435, 4350, 4351, 4352, 4353, 4358, 4359, 436, 437, 4370, 4371, 4372, 4373, 4374, 4375, 4376, 4377, 99702, 4378, 4379, 438, 4380, 4381, 43810, 43811, 43812, 43813, 43814, 43819, 4382, 43820, 43821, 43822, 4383, 43830, 43831, 43832, 4384, 43840, 43841, 43842, 4385, 43850, 43851, 43852, 4386, 4387, 4388, 43881, 43882, 43883, 43884, 43885, 43889, and 4389
Congestive heart failure	<i>Diagnosis codes (from index and previous admissions)</i> 39891, 428, 4280, 4281, 4282, 42820, 42821, 42822, 42823, 4283, 42830, 42831, 42832, 42833, 4284, 42840, 42841, 42842, 42843, 4289, 429, 4290, 4291, 4292, 4293, 4294, 4295, 4296, 4297, 42971, 42979, 4298, 42981, 42982, 42983, 42989, and 4299
Atrial fibrillation	<i>Diagnosis codes (from index and previous admissions)</i> 4273, 42731, 42732
Chronic obstructive pulmonary disease	<i>Diagnosis codes (from index and previous admissions)</i> 491, 4910, 4911, 4912, 49120, 49121, 49122, 4918, 4919, 492, 4920, 4928, 493, 4930, 49300, 49301, 49302, 4931, 49310, 49311, 49312, 4932, 49320, 49321, 49322, 4938, 49380, 49381, 49382, 4939, 49390, 49391, 49392, 494, 4940, 4941, and 496

(Continued)

TABLE E2. Continued

Baseline characteristic	International Classification of Diseases, 9th Edition, Clinical Modification codes
Chronic kidney disease	<p>Nondialysis-dependent</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>403, 4030, 40300, 40301, 4031, 40310, 40311, 4039, 40390, 40391, 404, 4040, 40400, 40401, 40402, 40403, 4041, 40410, 40411, 40412, 40413, 4049, 40490, 40491, 40492, 40493, 582, 5820, 5821, 5822, 5824, 5828, 58281, 58289, 5829, 583, 5830, 5831, 5832, 5834, 5836, 5837, 5838, 58381, 58389, 5839, 585, 5851, 5852, 5853, 5854, 5855, 5859, 586, 587, 588, 5880, 5881, 5888, 58881, 58888, 5889, V420, and V56</p> <p>Dialysis-dependent</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>V451, V4511, V4512, V560, V561, V562, V563, V5631, V5632, V568, and 5856</p>
Liver disease	<p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>070, 0700, 0701, 0702, 07020, 07021, 07022, 07023, 0703, 07030, 07031, 07032, 07033, 0704, 07041, 07042, 07043, 07044, 07049, 0705, 07051, 07052, 07053, 07054, 07059, 0706, 0707, 07070, 07071, 0709, 456, 4560, 4561, 4562, 45620, 45621, 4563, 4564, 4565, 4566, 4568, 570, 571, 5710, 5711, 5712, 5713, 5714, 57140, 57141, 57142, 57149, 5715, 5716, 5718, 5719, 572, 5720, 5721, 5722, 5723, 5724, 5728, 573, 5730, 5731, 5732, 5733, 5734, 5735, 5738, 5738, 7824, 7891, 7895, 78951, 78959, 7904, 7905, 7948, and V427</p>
Cancer	<p>Oropharyngeal cancers</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>140, 1400, 1401, 1403, 1404, 1405, 1406, 1408, 1409, 141, 1410, 1411, 1412, 1413, 1414, 1415, 1416, 1418, 1419, 142, 1420, 1421, 1422, 1428, 1429, 143, 1430, 1431, 1438, 1439, 144, 1440, 1441, 1448, 1449, 145, 1450, 1451, 1452, 1453, 1454, 1455, 1456, 1458, 1459, 146, 1460, 1461, 1462, 1463, 1464, 1465, 1466, 1467, 1468, 1469, 147, 1470, 1471, 1472, 1473, 1478, 1479, 148, 1480, 1481, 1482, 1483, 1488, 1489, 149, 1490, 1491, 1498, and 1499</p> <p>Gastrointestinal cancers</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>150, 1500, 1501, 1502, 1503, 1504, 1505, 1506, 1508, 1509, 1510, 151, 1511, 15012, 1513, 1514, 1515, 1516, 1518, 1519, 152, 1520, 1521, 1522, 1523, 1528, 1529, 153, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 154, 1540, 1541, 1542, 1543, 1548, 155, 1550, 1551, 1552, 156, 1560, 1561, 1562, 1568, 1569, 157, 1570, 1571, 1572, 1573, 1574, 1578, 1579, 158, 1580, 1588, 1589, 159, 1590, 1591, 1598, and 1599</p> <p>Respiratory tract cancers</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>160, 1600, 1601, 1602, 1603, 1604, 1605, 1608, 1609, 161, 1610, 1611, 1612, 1613, 1618, 1619, 162, 1620, 1622, 1623, 1624, 1625, 1628, 1629, 163, 1630, 1631, 1638, 1639, 164, 1640, 1461, 1462, 1463, 1468, 1649, 165, 1650, 1658, and 1659</p> <p>Bone and connective tissue cancer</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>170, 1700, 1701, 1702, 1703, 1704, 1705, 1706, 1707, 1708, 1709, 171, 1710, 1712, 1713, 1714, 1715, 1716, 1717, 1718, 1719, 172, 1720, 1721, 1722, 1723, 1724, 1725, 1726, 1727, 1728, 1729, 173, 1730, 17300, 17301, 17302, 17309, 1731, 17310, 17311, 17312, 17319, 1732, 17320, 17321, 17322, 17329, 1733, 17330, 17331, 17332, 17339, 1734, 17340, 17341, 17342, 17349, 1735, 17350, 17351, 17352, 17359, 1736, 17360, 17361, 17362, 17369, 1737, 17370, 17371, 17372, 17379, 1738, 17380, 17381, 17382, 17389, 1739, 17390, 17391, 17392, 17399, 174, 1740, 1741, 1742, 1743, 1744, 1745, 1746, 1748, 1749, 175, 1750, 1759, 176, 1760, 1761, 1762, 1763, 1764, 1765, 1768, and 1769</p> <p>Genitourinary cancers</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>179, 180, 1800, 1801, 1808, 1809, 181, 182, 1820, 1821, 1828, 183, 1830, 1832, 1833, 1834, 1835, 1838, 1839, 184, 1840, 1841, 1842, 1843, 1844, 1848, 1849, 185, 186, 1860, 1869, 187, 1871, 1872, 1873, 1874, 1875, 1876, 1877, 1878, 1879, 188, 1880, 1881, 1882, 1883, 1884, 1885, 1886, 1887, 1888, 1889, 189, 1890, 1891, 1892, 1893, 1894, 1898, and 1899</p> <p>Lymphoid cancers</p> <p><i>Diagnosis codes (from index and previous admissions)</i></p> <p>200, 2000, 20000, 20001, 20002, 20003, 20004, 20005, 20006, 20007, 20008, 2001, 20010, 20011, 20012, 20013, 20014, 20015, 20016, 20017, 20018, 2002, 20020, 20021, 20022, 20023, 20024, 20025, 20026, 20027, 20028, 2003, 20030, 20031, 20032, 20033, 20034, 20035, 20036, 20037, 20038, 2004, 20040, 20041, 20042, 20043, 20044, 20045, 20046, 20047, 20048, 2005, 20050, 20051, 20052, 20053, 20054, 20055, 20056, 20057, 20058,</p>

(Continued)

TABLE E2. Continued

Baseline characteristic	International Classification of Diseases, 9th Edition, Clinical Modification codes
	2006, 20060, 20061, 20062, 20063, 20064, 20065, 20066, 20067, 20068, 2007, 20070, 20071, 20072, 20073, 20074, 20075, 20076, 20076, 20077, 20078, 2008, 20080, 20081, 20082, 20083, 20084, 20085, 20086, 20087, 20088, 201, 2010, 20100, 20101, 20102, 20103, 20104, 20105, 20106, 20107, 20108, 2011, 20110, 20111, 20112, 20113, 20114, 20115, 20116, 20117, 20118, 2012, 20120, 20121, 20122, 20123, 20124, 20125, 20126, 20127, 20128, 2014, 20140, 20141, 20142, 20143, 20144, 20145, 20146, 20147, 20148, 2015, 20150, 20151, 20152, 20153, 20154, 20155, 20156, 20157, 20158, 2016, 20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168, 2017, 20170, 20171, 20172, 20173, 20174, 20175, 20176, 20177, 20178, 2019, 20190, 20191, 20192, 20193, 20194, 20195, 20196, 20197, 20198, 202, 2020, 20200, 20201, 20202, 20203, 20204, 20205, 20206, 20207, 20208, 2021, 20210, 20211, 20212, 20213, 20214, 20215, 20216, 20217, 20218, 2022, 20220, 20221, 20222, 20223, 20224, 20225, 20226, 20227, 20228, 2023, 20230, 20231, 20232, 20233, 20234, 20235, 20236, 20237, 20238, 2024, 20240, 20241, 20242, 20243, 20244, 20245, 20246, 20247, 20248, 2025, 20250, 20251, 20252, 20253, 20254, 20255, 20256, 20257, 20258, 2026, 20260, 20261, 20262, 20263, 20264, 20265, 20266, 20267, 20268, 2027, 20270, 20271, 20272, 20273, 20274, 20275, 20276, 20277, 20278, 2028, 20280, 20281, 20282, 20283, 20284, 20285, 20286, 20287, 20288, 2029, 20290, 20291, 20292, 20293, 20294, 20295, 20296, 20297, 20298, 203, 2030, 20300, 20301, 20302, 2031, 20310, 20311, 20312, 2038, 20380, 20381, and 20382
	Hematologic cancers
	<i>Diagnosis codes (from index and previous admissions)</i>
	204, 2040, 20400, 20401, 20402, 2041, 20410, 20411, 20412, 2042, 20420, 20421, 20422, 2048, 20480, 20481, 20482, 2049, 20490, 20491, 20492, 205, 2050, 20500, 20501, 20502, 2051, 20510, 20511, 20512, 2052, 20520, 20521, 20522, 2053, 20530, 20531, 20532, 2058, 20580, 20581, 20582, 2059, 20590, 20591, 20592, 206, 2060, 20600, 20601, 20602, 2061, 20610, 20611, 20612, 2062, 20620, 20621, 20622, 2068, 20680, 20681, 20682, 2069, 20690, 20691, 20692, 207, 2070, 20700, 20701, 20702, 2071, 20710, 20711, 20712, 2072, 20720, 20721, 20722, 2078, 20780, 20781, 20782, 208, 2080, 20800, 20801, 20802, 2081, 20810, 20811, 20812, 2082, 20820, 20821, 20822, 2088, 20880, 20881, 20882, 2089, 20890, 20891, 20892, 209, 2090, 20900, 20901, 20902, 20903, 2091, 20910, 20911, 20912, 20913, 20914, 20915, 20916, 20917, 2092, 20920, 20921, 20922, 20923, 20924, 20925, 20926, 20927, 20929, 2093, 20930, 20931, 20932, 20933, 20934, 20935, 20936, 2094, 20940, 20941, 20942, 20943, 2095, 20950, 20951, 20952, 20953, 20954, 20955, 20956, 20957, 2096, 20960, 20961, 20962, 20963, 20964, 20965, 20966, 20967, 20969, 2097, 20970, 20971, 20972, 20973, 20974, 20975, and 20979
	Other cancers
	<i>Diagnosis codes (from index and previous admissions)</i>
	190, 1900, 1901, 1902, 1903, 1904, 1905, 1906, 1907, 1908, 1909, 191, 1910, 1911, 1912, 1913, 1914, 1915, 1916, 1917, 1918, 1919, 192, 1920, 1921, 1922, 1923, 1928, 1929, 193, 194, 1940, 1941, 1943, 1944, 1945, 1946, 1948, 195, 1950, 1951, 1952, 1953, 1954, 1955, 1958, 196, 1960, 1961, 1962, 1963, 1965, 1966, 1968, 1969, 197, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 198, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 19881, 19882, 19889, 199, 1990, 1991, and 1992

TABLE E3. Definition of secondary endpoints

Outcome	International Classification of Diseases, 9th Edition, Clinical Modification codes
Stroke	<p>Iatrogenic stroke</p> <p><i>Diagnosis code (from index hospitalization)</i></p> <p>99702</p> <p>Hemorrhagic stroke</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admissions)</i></p> <p>430, 431, 432, 4320, 4321, and 4329</p> <p>Ischemic stroke</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admissions)</i></p> <p>43301, 43311, 43321, 43331, 43381, 43391, 43401, 43411, and 43491</p>
Reoperation	<p><i>Procedure codes (subsequent admissions)</i></p> <p>3523 and 3524</p>
Major bleeding event	<p>Intracerebral hemorrhage</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>430, 431, 432, 4320, 4321, and 4329</p> <p>Hemopericardium or cardiac tamponade</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>4230 and 4233</p> <p>Gastrointestinal hemorrhage</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>4560, 45620, 4590, 53021, 5310, 53100, 53101, 5312, 53120, 53121, 5314, 53140, 53141, 5316, 53160, 53161, 5320, 53200, 53201, 5322, 53220, 53221, 53241, 5326, 53260, 53261, 5330, 53300, 53301, 5332, 53320, 53321, 53340, 533401, 5336, 53360, 53361, 5340, 53400, 53401, 5342, 53420, 53421, 5344, 53440, 53441, 5346, 53501, 53511, 53521, 53531, 53541, 53561, 53571, 5693, 578, 5780, 5781, and 5789</p> <p>Hematuria</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>5997, 59970, and 59971</p> <p>Hemarthrosis</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>7191, 71910, 71911, 71912, 71913, 71914, 71915, 71916, 71917, 71918, and 71919</p> <p>Hemoptysis</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>7848, 7863, 78630, and 78639</p> <p>Epistaxis</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>7847</p> <p>Retinal or choroidal hemorrhage</p> <p><i>Diagnosis codes (primary diagnosis of subsequent admission)</i></p> <p>36281, 36243, 36361, and 36362</p>

TABLE E4. Definition of 30-day complications

Outcome	International Classification of Diseases, 9th Edition, Clinical Modification codes
Stroke	<p><i>Diagnosis code (from index admission)</i> 99702</p> <p><i>Diagnosis codes (from subsequent admissions)</i> 430, 431, 432, 4320, 4321, 4329, 43301, 43311, 43321, 43331, 43381, 43391, 43401, 43411, and 43491</p>
Atrial fibrillation	<p><i>Diagnosis code (from index and subsequent admissions)</i> 4273, 42731, and 42732</p>
Acute kidney injury	<p><i>Diagnosis code (from index and subsequent admissions)</i> 5939, 584, 5845, 5846, 5847, 5848, and 5849</p>
Respiratory failure	<p>Respiratory arrest <i>Diagnosis codes (from index and subsequent admissions)</i> 7991</p> <p>Pulmonary insufficiency <i>Diagnosis codes (from index and subsequent admissions)</i> 5185, 51881, 51882, and 51884</p> <p>Pulmonary collapse <i>Diagnosis codes (from index and subsequent admissions)</i> 5180</p> <p>Lung edema <i>Diagnosis codes (from index and subsequent admissions)</i> 5184, 2766, 27661, and 27669</p> <p>Pneumothorax <i>Diagnosis codes (from index and subsequent admissions)</i> 5120, 5121, and 5122</p> <p>Pulmonary embolism <i>Diagnosis codes (from index and subsequent admissions)</i> 4151, 41511, 41512, 41513, and 41519</p> <p>Pneumonia <i>Diagnosis codes (from index and subsequent admissions)</i> 00322, 0203, 0204, 0205, 0212, 0221, 0310, 0391, 0521, 0551, 0730, 0830, 1124, 1140, 1144, 1145, 11505, 11515, 11595, 1304, 1363, 4800, 4801, 4802, 4803, 4808, 4809, 481, 4820, 4821, 4822, 4823, 48230, 48231, 48232, 48239, 4824, 48240, 48241, 48242, 48249, 4828, 48281, 48282, 48283, 48284, 48289, 4829, 483, 4830, 4831, 4838, 4841, 4843, 4845, 4846, 4847, 4848, 485, 486, 5130, and 5171</p> <p>Postoperative tracheostomy <i>Procedure codes (from index admission)</i> 311, 312, 3121, 3129</p> <p>Continuous mechanical ventilation for 96 consecutive hours or more or unspecified duration <i>Procedure codes (from index admission)</i> 9670 and 9672</p> <p>Reintubation <i>Procedure codes (from index admission)</i> 9604</p>

TABLE E5. Multivariable Cox regression analysis results of each endpoint in the full study cohort: survival, stroke, major bleeding, and reoperation

Variable	Hazard ratio	95% confidence interval	P value
Survival			
Bioprosthesis	1.39	1.05-1.83	.02
Age	1.02	1.01-1.03	.009
Male sex	0.94	0.77-1.14	.51
Race			
White	1.00	—	—
African-American	1.20	0.95-1.52	.13
Other	0.82	0.66-1.02	.07
Emergent/urgent admission	1.08	0.89-1.32	.43
NY State residency	0.81	0.66-1.00	.05
Coagulation/platelet disorders	1.06	0.68-1.64	.80
Hypertension	1.61	1.27-2.03	<.001
Diabetes mellitus	1.41	1.06-1.88	.02
Coronary artery disease	1.32	1.04-1.67	.02
Peripheral vascular disease	1.96	1.27-3.02	.003
Cerebrovascular disease	1.02	0.75-1.39	.89
Congestive heart failure	1.23	0.99-1.51	.06
Atrial fibrillation	1.12	0.93-1.34	.24
Chronic obstructive pulmonary disease	1.92	1.60-2.30	<.001
Dialysis dependency	3.70	2.60-5.26	<.001
Liver disease	1.44	0.98-2.10	.06
Cancer	3.34	2.18-5.13	<.001
Year of surgery	0.94	0.90-0.97	<.001
Stroke			
Bioprosthesis	0.87	0.60-1.27	.47
Age	1.01	0.99-1.03	.20
Male sex	0.80	0.60-1.08	.15
Race			
White	1.00	—	—
African-American	1.42	1.04-1.94	.03
Other	1.16	0.83-1.62	.40
Emergent/urgent Admission	0.88	0.64-1.22	.45
NY State residency	0.64	0.50-0.83	<.001
Coagulation/platelet disorders	1.25	0.66-2.37	.49
Hypertension	1.65	1.21-2.25	.001
Diabetes mellitus	1.38	0.87-2.21	.18
Coronary artery disease	0.94	0.67-1.33	.74
Peripheral vascular disease	0.56	0.13-2.35	.43
Cerebrovascular disease	1.64	1.04-2.57	.03
Congestive heart failure	1.34	1.02-1.78	.04
Atrial fibrillation	1.02	0.80-1.30	.88
Chronic obstructive pulmonary disease	1.28	0.94-1.74	.12
Dialysis dependent	1.05	0.50-2.23	.90
Liver disease	0.67	0.35-1.27	.22
Cancer	1.70	0.78-3.69	.18
Year of surgery	1.02	0.97-1.07	.46
Major bleeding			
Bioprosthesis	0.72	0.46-1.12	.15
Age	1.03	1.00-1.05	.02
Male sex	0.72	0.53-0.97	.03

(Continued)

TABLE E5. Continued

Variable	Hazard ratio	95% confidence interval	P value
Race			
White	1.00	—	—
African-American	0.94	0.63-1.41	.78
Other	1.13	0.86-1.50	.37
Emergent/urgent admission	0.95	0.68-1.32	.75
NY State residency	0.87	0.67-1.13	.28
Coagulation/platelet disorders	1.44	0.90-2.31	.13
Hypertension	1.17	0.87-1.57	.31
Diabetes mellitus	1.54	1.00-2.37	.05
Coronary artery disease	0.90	0.63-1.29	.58
Peripheral vascular disease	1.76	0.84-3.68	.13
Cerebrovascular disease	1.45	0.90-2.34	.13
Congestive heart failure	1.65	1.20-2.28	.003
Atrial fibrillation	0.95	0.73-1.23	.68
Chronic obstructive pulmonary disease	1.24	0.93-1.64	.14
Dialysis dependent	2.74	1.59-4.74	<.001
Liver disease	1.20	0.73-1.95	.48
Cancer	2.03	1.04-3.94	.38
Year of surgery	0.98	0.94-1.03	.44
Mitral reoperation			
Bioprosthesis			
5 y	3.39	2.35-4.89	<.001
10 y	6.43	3.99-10.4	<.001
15 y	12.2	5.77-25.8	<.001
Age	0.97	0.95-0.98	<.001
Male sex	0.89	0.64-1.22	.46
Race			
White	1.00	—	—
African-American	1.05	0.68-1.61	.84
Other	0.60	0.43-0.85	.003
Emergent/urgent admission	1.01	0.72-1.42	.94
NY State residency	0.94	0.68-1.31	.73
Coagulation/platelet disorders	1.53	0.79-2.95	.21
Hypertension	1.57	1.11-2.20	.01
Diabetes mellitus	0.60	0.28-1.29	.19
Coronary artery Disease	1.33	0.87-2.03	.19
Peripheral vascular disease	2.00	0.66-6.10	.22
Cerebrovascular disease	0.70	0.36-1.35	.29
Congestive heart failure	0.85	0.63-1.15	.29
Atrial fibrillation	0.93	0.64-1.34	.68
Chronic obstructive pulmonary disease	0.98	0.59-1.63	.95
Dialysis dependent	2.12	1.06-4.24	.03
Liver disease	0.61	0.28-1.35	.23
Cancer	1.80	0.81-4.03	.15
Year of surgery	1.01	0.94-1.08	.89

TABLE E6. Patient baseline characteristics in the overall cohort and by type of prosthesis

Baseline characteristics	Prosthesis type, n (%)			Standardized difference (%)	P value
	All patients (N = 2727)	Bioprosthetic (n = 382)	Mechanical (n = 2345)		
Demographics					
Age, median [IQR], y	43 [38-47]	42 [36-47]	43 [38-47]	17.4	.005
18-30	237 (8.7)	52 (13.6)	185 (7.9)		.001
31-40	750 (27.5)	101 (26.4)	649 (27.7)		
41-50	1740 (63.8)	229 (59.9)	1511 (64.4)		
Men	1076 (39.5)	143 (37.4)	933 (39.8)	4.8	.38
New York State resident	1293 (47.4)	216 (56.5)	1077 (45.9)	21.4	<.001
Race/ethnicity					
White (non-Hispanic)	1437 (52.7)	188 (49.2)	1249 (53.3)	8.1	.09
African-American (non-Hispanic)	416 (15.3)	72 (18.8)	344 (14.7)	11.2	
Other	874 (32.0)	122 (31.9)	752 (32.1)	0.3	
Emergent/urgent admission	772 (28.3)	149 (39.0)	623 (26.6)	26.7	<.001
Comorbidities					
Coagulation/platelet disorders	112 (4.1)	20 (5.2)	92 (3.9)	6.3	.23
Hypertension	791 (29.0)	103 (27.0)	688 (29.3)	5.3	.34
Diabetes mellitus	188 (6.9)	28 (7.3)	160 (6.8)	2.0	.72
Coronary artery disease	433 (15.9)	69 (18.1)	364 (15.5)	6.8	.21
Peripheral vascular disease	48 (1.8)	6 (1.6)	42 (1.8)	1.7	.76
Cerebrovascular disease	165 (6.1)	30 (7.9)	135 (5.8)	8.3	.11
Congestive heart failure	1329 (48.7)	193 (50.5)	1136 (48.4)	4.2	.45
Atrial fibrillation	910 (33.4)	94 (24.6)	816 (34.8)	22.4	<.001
Chronic obstructive pulmonary disease	417 (15.3)	70 (18.3)	347 (14.8)	9.5	.08
Chronic kidney disease	154 (5.6)	26 (6.8)	128 (5.5)	5.6	.29
Dialysis dependent	114 (4.2)	17 (4.5)	97 (4.1)	1.6	.78
Liver disease	148 (5.4)	22 (5.8)	126 (5.4)	1.7	.76
Cancer	64 (2.3)	14 (3.7)	50 (2.1)	9.2	.07
Year of surgery					
1997	346 (12.7)	35 (9.2)	311 (13.3)	13.0	<.001
1998	313 (11.5)	22 (5.8)	291 (12.4)	23.3	
1999	291 (10.7)	28 (7.3)	263 (11.2)	13.4	
2000	262 (9.6)	39 (10.2)	223 (9.5)	2.4	
2001	287 (10.5)	43 (11.3)	244 (10.4)	2.7	
2002	294 (10.8)	35 (9.2)	259 (11.0)	6.3	
2003	264 (9.7)	28 (7.3)	236 (10.1)	9.7	
2004	233 (8.5)	56 (14.7)	177 (7.5)	22.8	
2005	245 (9.0)	63 (16.5)	182 (7.8)	27.0	
2006	192 (7.0)	33 (8.6)	159 (6.8)	7.0	

IQR, Interquartile range.