Predictors of outcomes in patients with obesity following mitral valve surgery

Ahmed Alnajar, MD, MSPH,[a,b] Kelley N. Benck, BS,[a] Tawseef Dar, MD,[a] Sameer A. Hirji, MD, MPH,[c] Walid Ibrahim, MD,[a] Brian Detweiler, MS,[b] Venkat Vuddanda, MD, MS,[c] Raymond Balise, PhD,[b] J. Sunil Rao, PhD,[b] Min Lu, PhD,[b] and Joseph Lamelas, MD[a]

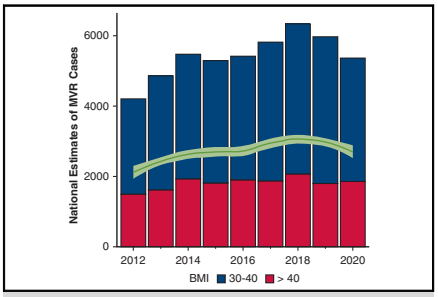
ABSTRACT

Objective: Few studies have assessed the outcomes of mitral valve surgery in patients with obesity. We sought to study factors that determine the in-hospital outcomes of this population to help clinicians provide optimal care.

Methods: A retrospective analysis of adult patients with obesity who underwent open mitral valve replacement or repair between January 1, 2012, and December 31, 2020, was conducted using the National Inpatient Sample. Weighted logistic regression and random forest analyses were performed to assess factors associated with mortality and the interaction of each variable.

Results: Of the 48,775 patients with obesity, 34% had morbid obesity (body mass index ≥40), 55% were women, 66% underwent elective surgery, and 55% received isolated open mitral valve replacement or repair. In-hospital mortality was 5.0% (n = 2430). After adjusting for important covariates, a greater risk of mortality was associated with older patients (adjusted odds ratio [aOR], 1.24; 95% CI, 1.08-1.43), higher Elixhauser comorbidity score (aOR, 2.10; 95% CI, 1.87-2.36), prior valve surgery (aOR, 1.63; 95% CI, 1.01-2.63), and more than 2 concomitant procedures (aOR, 2.83; 95% CI, 2.07-3.85). Lower mortality was associated with elective admissions (aOR, 0.70; 95% CI, 0.56-0.87) and valve repair (aOR, 0.58; 95% CI, 0.46-0.73). Machine learning identified several interactions associated with early mortality, such as Elixhauser score, female sex, body mass index ≥40, and kidney failure.

Conclusions: The complexity of presentation, comorbidities in older and female patients, and morbid obesity are independently associated with an increased risk of mortality in patients undergoing open mitral valve replacement or repair. Morbid obesity and sex disparity should be recognized in this population, and physicians should consider older patients and females with multiple comorbidities for earlier and more opportune treatment windows. (JTCVS Open 2023;15:127-50)



National trends of mitral valve surgery and obesity (2012-2020).

CENTRAL MESSAGE

Mortality risk after mitral surgery in patients with obesity can be improved by better clinical management of comorbidities.

PERSPECTIVE

Patients with obesity are at increased risk of morbidity and mortality, especially older and female patients with multiple comorbidities. Thus, addressing the modifiable factors associated with mortality in these patients could offer clinicians the chance to tailor their pre- and postoperative care for more optimal outcomes following mitral valve surgery.

Patients undergoing cardiac surgery are increasingly presenting with obesity. Previous studies have shown that obesity is an independent risk factor for cardiovascular diseases.[1,2] In addition, patients with obesity, and particularly those with morbid obesity, pose significant technical challenges to the surgical teams responsible for their care. Studies on the influence of obesity on mortality in cardiac surgery have predominantly looked into outcomes of coronary artery bypass grafting (CABG).[3,4] However, mitral valve (MV) disease has been reported as one of the most common valvular lesion in the United States,[5] and surgery is currently the only available treatment for patients with severe MV disease.

Only a few studies have examined the outcomes of MV surgery in this population, and they did not provide clear

From the [a]Division of Cardiothoracic Surgery, DeWitt Daughtry Department of Surgery, and [b]Division of Biostatistics, Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, Fla; and [c]Division of Cardiothoracic Surgery, Brigham and Women's Hospital, Allston, Mass.

The study did not involve living human subjects or accessing identifiable information or identifiable biospecimens. For this reason, our human Subject Research Office determined that this study does not require institutional review board review, approval, or oversight.

Read at The American Association for Thoracic Surgery Mitral Conclave Workshop, Boston, Massachusetts, May 13-14, 2022.

Received for publication Sept 18, 2022; revisions received March 4, 2023; accepted for publication March 13, 2023; available ahead of print July 19, 2023.

Address for reprints: Ahmed Alnajar, MD, MSPH, Division of Cardiothoracic Surgery, Department of Surgery, University of Miami Miller School of Medicine, 1295 NW 14th St, Suite J, Miami, FL 33125 (E-mail: alnajarmd@gmail.com).

2666-2736

https://doi.org/10.1016/j.xjon.2023.03.017

Abbreviations and Acronyms

BMI = body mass index
bRF = balanced random forest
CABG = coronary artery bypass grafting
CHF = congestive heart failure
CKD = chronic kidney disease
HCUP = Health Care Cost and Utilization Project
ICD = International Classification of Diseases
LOS = length of stay
MV = mitral valve
NIS = Nationwide Inpatient Sample

and specific results.[6-8] However, optimal hospital care requires an in-depth understanding of the complex factors influencing surgical outcomes for more accurate, precise, and impactful management during hospitalization and after discharge, especially for high-risk patients. The main purpose of our study is to identify the factors associated with mortality in patients with obesity who underwent MV surgery, including the severity of obesity itself (Figure 1). To provide detailed information that accounts for individual variability, we used robust machine learning tools to study national outcomes for patients with obesity undergoing MV surgery.

METHODS

Data Source

A retrospective analysis was conducted using discharge data from the Health Care Cost and Utilization Project's (HCUP) National Inpatient Sample (NIS). The NIS is the largest publicly available all-payer database of hospitalized patients in the United States and is sponsored by the Agency for Healthcare Research and Quality. Annually, NIS collects sampled anonymized data on discharge diagnoses and procedures from more than 7 million hospitalizations. The NIS dataset constitutes a 20% stratified sample of US hospitals and provides sampling weights to calculate national estimates that represent more than 95% of the US population. This study was considered exempt from institutional review board approval because the NIS de-identifies patient information.

Study Population

This study included adult (aged 18 years and older) patients with obesity who underwent open MV surgery from January 1, 2012, to December 31, 2020. Patient characteristics and procedure details were identified using the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) codes. A summary of the relevant ICD codes is in Table E1. Our study included all patients who underwent MV surgery during their hospitalization and were diagnosed with obesity, which was classified using body mass index (BMI) >30. We carefully assessed each of the ICD codes and excluded patients who underwent catheter-based mitral intervention.

Study Outcomes

The primary outcome of interest was in-hospital mortality. Secondary outcomes included perioperative complications (such as acute myocardial infarction, stroke, major bleeding, and acute kidney injury [determined

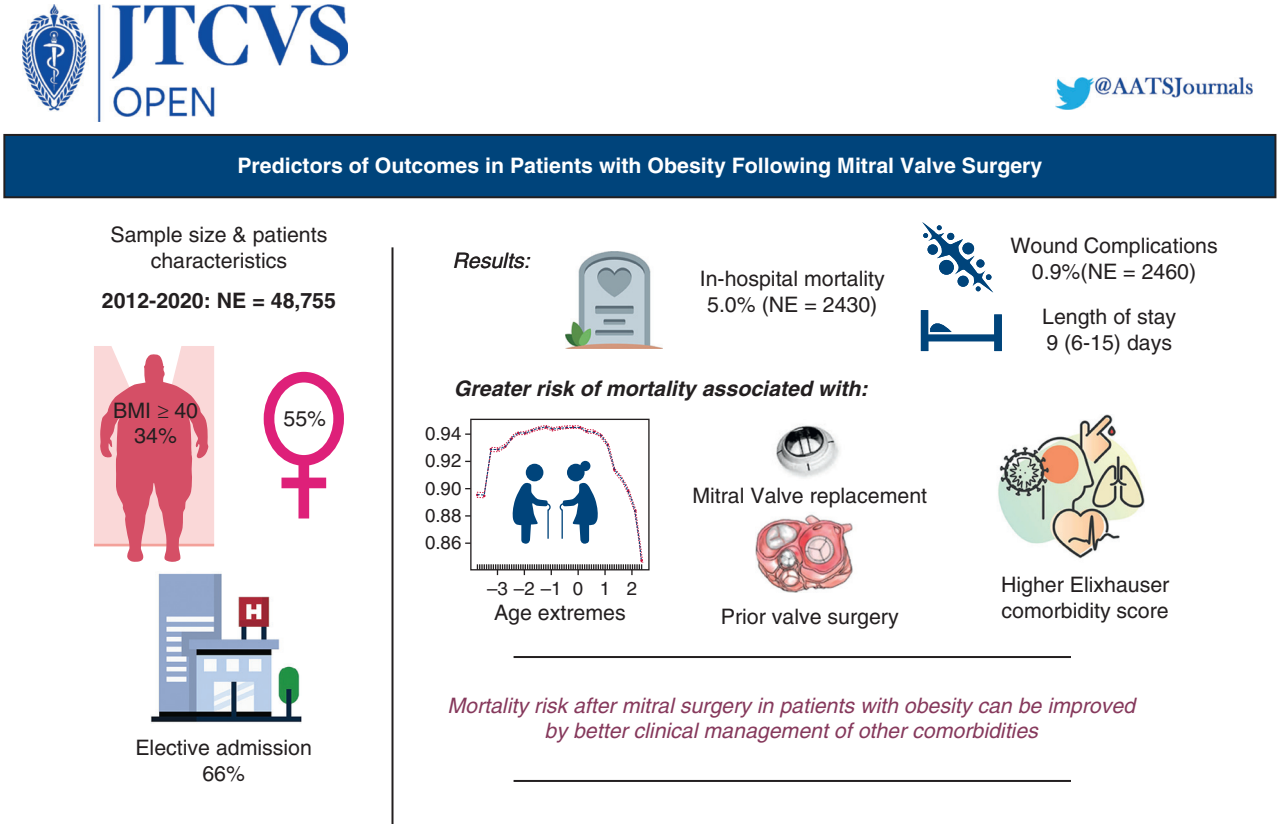


FIGURE 1. Graphical abstract. *NE*, National estimate; *BMI*, body mass index.

TABLE 1. Baseline characteristics

Characteristic	Overall (N = 48,775)	Patients with obesity		*P* value*
		BMI 30-39 (n = 32,430)	BMI ≥40 (n = 16,345)	
Age (y)	64 (55-71)	65 (56-72)	62 (53-69)	**<.001**
Age group (y)				**<.001**
18-49	7115 (15)	4095 (13)	3020 (18)	
50-64	18,745 (38)	12,075 (37)	6670 (41)	
65-79	21,010 (43)	14,600 (45)	6410 (39)	
80+	1905 (3.9)	1660 (5.1)	245 (1.5)	
Sex				**<.001**
Female	26,600 (55)	15,835 (49)	10,765 (66)	
Male	22,170 (45)	16,595 (51)	5575 (34)	
Unknown	5	0	5	
Race/ethnicity				**<.001**
White	34,350 (74)	23,150 (75)	11,200 (72)	
Black	6275 (14)	3695 (12)	2580 (17)	
Hispanic	3395 (7.4)	2340 (7.6)	1055 (6.8)	
Asian or Pacific Islander	730 (1.6)	510 (1.7)	220 (1.4)	
Native American	245 (0.5)	135 (0.4)	110 (0.7)	
Other	1165 (2.5)	840 (2.7)	325 (2.1)	
Unknown	2615	1760	855	
Weighted Elixhauser Comorbidity index	12 ± 9	11 ± 9	14 ± 9	**<.001**
HTN	32,890 (67)	22,275 (69)	10,615 (65)	**<.001**
DM	18,585 (38)	11,465 (35)	7120 (44)	**<.001**
Dyslipidemia	28,020 (57)	19,820 (61)	8200 (50)	**<.001**
Previous MI	3760 (7.7)	2750 (8.5)	1010 (6.2)	**<.001**
CAD	18,390 (38)	12,880 (40)	5510 (34)	**<.001**
PAD	3375 (6.9)	2360 (7.3)	1015 (6.2)	**.047**
COPD	18,385 (38)	11,515 (36)	6870 (42)	**<.001**
Afib	30,065 (62)	20,035 (62)	10,030 (61)	.7
TIA	2245 (4.6)	1510 (4.7)	735 (4.5)	.7
Stroke	3835 (7.9)	2365 (7.3)	1470 (9.0)	**.003**
CKD	12,720 (26)	7720 (24)	5000 (31)	**<.001**
End-stage CKD	2050 (4.2)	1190 (3.7)	860 (5.3)	**<.001**
CHF admission	1115 (2.3)	660 (2.0)	455 (2.8)	**.018**
CHF	30,735 (63)	19,690 (61)	11,045 (68)	**<.001**
Redo	3040 (6.2)	2275 (7.0)	765 (4.7)	**<.001**
Previous PCI	3485 (7.1)	2510 (7.7)	975 (6.0)	**.001**
MV repair	20,340 (42)	14,745 (45)	5595 (34)	**<.001**
Elective admission	32,340 (66)	22,275 (69)	10,065 (62)	**<.001**
Unknown	115	55	60	
Concomitant procedures				**<.001**
Isolated MV repair	26,960 (55)	18,035 (56)	8925 (55)	
+CABG	6825 (14)	4975 (15)	1850 (11)	
+AVR	6540 (13)	4135 (13)	2405 (15)	
+AscendingAo	265 (0.5)	130 (0.4)	135 (0.8)	
+TVR	4855 (10.0)	2935 (9.1)	1920 (12)	
>2 procedures	3330 (6.8)	2220 (6.8)	1110 (6.8)	
LAAL/maze	17,650 (36)	11,740 (36)	5910 (36)	>.9

Values are presented as median (interquartile range), n (%), or mean ± SD. Bold indicates $P < .05$. *BMI*, Body mass index; *HTN*, hypertension; *DM*, diabetes; *MI*, myocardial infarction; *CAD*, coronary artery disease; *PAD*, peripheral arterial disease; *COPD*, chronic obstructive pulmonary disease; *Afib*, atrial fibrillation; *TIA*, transient ischemic attack; *CKD*, chronic kidney disease; *CHF*, congestive heart failure; *CABG*, coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *Redo*, reoperation after previous CABG or valve surgery; *MV*, mitral valve; *AVR*, aortic valve replacement; *AscendingAo*, aortic surgery; *TVR*, tricuspid valve replacement; *LAAL*, left atrial appendage ligation.
*Wilcoxon rank-sum test for complex survey samples and χ^2 test with Rao and Scott second-order correction.

TABLE 2. In-hospital outcomes stratified by patients' body mass index (BMI) category

Characteristic	Overall (N = 48,775)	Patients with obesity		*P* value*
		BMI 30-39 (n = 32,430)	BMI ≥40 (n = 16,345)	
In-hospital mortality	2430 (5.0)	1150 (3.5)	1280 (7.8)	**<.001**
Unknown	20	10	10	
Wound complications	460 (0.9)	235 (0.7)	225 (1.4)	**.002**
Valve complications	1045 (2.1)	645 (2.0)	400 (2.4)	.14
Bleeding complications	26,580 (54)	17,785 (55)	8795 (54)	.3
Transfusion	11,535 (24)	7615 (23)	3920 (24)	.6
Complete heart block	7230 (15)	4840 (15)	2390 (15)	.7
Cardiac arrest	2630 (5.4)	1755 (5.4)	875 (5.4)	>.9
Permanent stroke	255 (0.5)	160 (0.5)	95 (0.6)	.6
Perioperative MI	3545 (7.3)	2405 (7.4)	1140 (7.0)	.4
Acute renal failure	14,910 (31)	8525 (26)	6385 (39)	**<.001**
CIED	220 (0.5)	150 (0.5)	70 (0.4)	.8
Permanent pacemaker	11,610 (24)	7660 (24)	3950 (24)	.6

Values are presented as n (%). Bold indicates $P < .05$. *MI*, Myocardial infarction; *CIED*, implantable cardioverter defibrillator. *$\chi 2$ test with Rao & Scott second-order correction.

based on the secondary diagnoses of the NIS database]), discharge disposition, hospital length of stay (LOS), and hospitalization cost.

Analysis Methods

Using survey analysis methods, we generated weighted national estimates and variances that accounted for the clustering of outcomes within hospitals and sampling variation across strata (region and year) as recommended by Agency for Healthcare Research and Quality to describe patients' characteristics and outcomes (Online Data Supplement).[9] Observation weight was then incorporated into subsequent models.

Descriptive statistics were presented as frequencies for categorical variables and averages ± SD or medians (interquartile range) for continuous variables. Normality was visually assessed with histograms and QQ plots. The χ^2 and Wilcoxon rank-sum tests for survey samples were used to compare groups. To determine which risk factors were associated with in-hospital mortality, we used logistic regression and machine learning. For the descriptive analysis, the whole cohort was included, and the missing values of each variable were presented in their own categories. Only a few observations (unweighted n = 4) were omitted at the stage of predictive modeling for missing the outcome variable "mortality." Imputation of other missing variables was performed by chaining random forests with multiple imputations that consider observation weights. Candidate variables from the NIS were selected based on a literature review. The Elixhauser comorbidity index was used to indicate the severity of patient presentation.

Univariable weighted logistic regression models assessed each variable of interest individually, and the adjusted model was the final logistic regression model used after multicollinearity assessment (with the variance inflation factor) and z score transformation (for continuous variables). To assess our model's performance with and without the Elixhauser comorbidity index, a sensitivity analysis was conducted (Table E2).

Because developing risk prediction models for patients with obesity and identifying high-risk individuals is a challenging task and studies have yielded mixed results,[3,4,10,11] we decided to explore variables' association with mortality by a completely nonparametric classification model—independent from the logistic model, with the same variables—using random forest methodology. This method helps researchers uncover complex interactions and reduce the number of variables from large datasets. Furthermore, balanced random forests (bRF) can provide a path for analyzing class-imbalanced data[12] that frequently get overlooked in data-driven analyses, especially with HCUP datasets.[13] Thus, we used weighted bRF to evaluate the importance and interaction of each variable.

The analysis was performed using R version 4.2.2 (R Foundation for Statistical Computing) with multiple packages, including *gtsummary*, *survey*, and *randomForestSRC* (Table E3). Significant associations from statistical models were determined using $\alpha = 0.05$. For reproducibility and further details,[14] the analysis code and output knitted from the R Markdown file can be accessed in the Online Data Supplement.

RESULTS

The sample included 9755 encounters that were weighted to represent 48,775 patients nationally. These patients had obesity (BMI ≥30) and underwent MV surgery between 2012 and 2020. There was a trend of an increased number of patients with obesity over this period (Figure 2).

Patient Characteristics

Among patients with obesity, more than half (55% [n = 26,600]) were women, and more than one-third (34% [n = 16,345]) had morbid obesity (BMI ≥40). There were fewer women with BMI ≥40 than those with BMI <40 (40% vs 60%, respectively); however, more women than men had BMI ≥40 (66% vs 44%, respectively). The mean Elixhauser score was 12 ± 9, which increased in patients with morbid obesity (14 ± 9 vs 11 ± 9 in patients with BMI ≥40 and BMI <40, respectively). The most common other comorbidities were hypertension (67%), congestive heart failure (63%), and atrial fibrillation (62%). Most patients underwent MV replacement (only 42% repair), 66% underwent elective surgery, and 55% underwent isolated MV surgery. The most common major concomitant surgery was CABG (14%), followed by aortic valve replacement

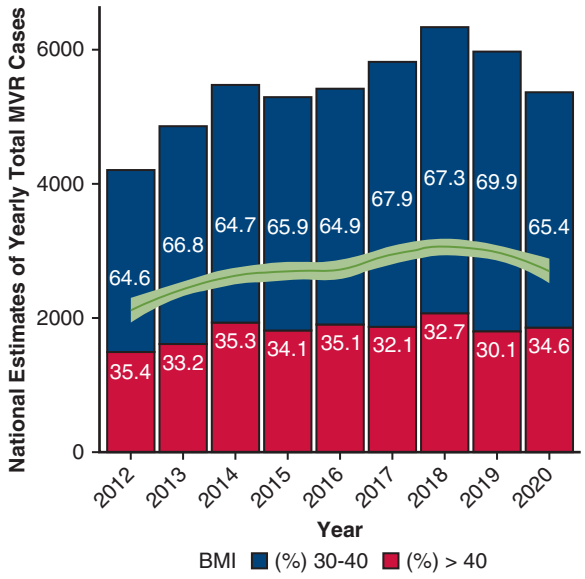


FIGURE 2. Temporal trend of patients with obesity underwent mitral valve surgery in the United States between 2012 and 2020. *MVR*, Mitral valve surgery; *BMI*, body mass index.

(13%). A comparison of patients with morbid obesity was made for all comorbidities and surgeries in Table 1.

Primary Outcome

There were 2430 patients who died during their index admission. Overall in-hospital mortality was 5.0% (Table 2), which was higher in patients with morbid obesity (7.8% vs 3.5% in patients with BMI ≥40 and BMI <40, respectively; $P < .001$). In-hospital mortality for isolated MV surgery accounted for 3.2%, which increased up to 13% in concomitant surgery with more than 2 procedures (Table E4).

Predictors of mortality. After removing observations that were missing mortality status, the final sample was comprised of 9751 encounters with a nationally weighted estimate of 48,755 patients. We present the logistic model results followed by the random forest.

Logistic regression. Our weighted multivariable logistic regression model yielded an area under curve of 0.826, a Brier score of 0.042, a sensitivity of 0.753, a specificity of 0.753 (under a threshold of 0.049), and a range of variance inflation factor from 1.087 to 2.755 (Table 3).

Basic characteristics. In the unadjusted model, older age was a risk factor for mortality of patients with obesity (age z score odds ratio [OR], 1.24; 95% CI, 1.13-1.37; $P < .001$). However, when age groups were compared, octogenarian patients did not have significantly different mortality risk than patients aged 50 to 64 years (OR, 1.32; 95% CI, 0.84-2.07; $P = .2$). In the final adjusted model, age z score remains significant after adjustment for other variables (adjusted OR [aOR], 1.24; 95% CI, 1.08-1.43; $P = .002$). Compared with male patients, female patients had a greater risk of in-hospital mortality (OR, 1.24; 95% CI, 1.03-1.49; $P = .026$), but this risk was not significant after adjusting for other variables (aOR, 1.08; 95% CI, 0.87-1.33; $P = .05$). There was no evidence of race/ethnicity disparities, but there was evidence of health access disparities in the unadjusted model based on patient's insurance. Income above 150% federal poverty level was a significant protective factor (aOR, 0.75; 95% CI, 0.57-0.99; $P = .041$) after adjustment for other variables.

Comorbidities. A 1-point increase on the z scale of the Elixhauser comorbidity index was associated with more than a 2-fold increase in the risk of death (aOR, 2.10; 95% CI, 1.87-2.36; $P < .001$). Morbid obesity increased the risk of mortality by 80% (aOR, 1.80; 95% CI, 1.46-2.22; $P < .001$). Certain cardiac-related comorbidities, such as dyslipidemia and atrial fibrillation ($P < .05$) were found to have lower risk of mortality in the final model. Furthermore, admission for congestive heart failure (CHF) and end-stage chronic kidney disease (CKD) did not increase the risk of mortality in the final model. Patients who underwent reoperative cardiac surgery (redo) were only at higher risk of mortality following previous valve surgery in the adjusted model (aOR, 1.63; 95% CI, 1.01-2.63; $P = .044$).

Operative characteristics. Elective admission reduced the risk of mortality (aOR, 0.70; 95% CI, 0.56-0.87; $P < .001$). MV repair was a significant protective factor, compared with replacement, decreasing mortality risk by 42% (aOR, 0.58; 95% CI, 0.46-0.73; $P < .001$). Most concomitant surgeries had a higher risk of mortality than isolated MV surgery. CABG increased the risk by 66% (aOR, 1.66; 95% CI, 1.22-2.25; $P < .001$), aortic valve by 82% (aOR, 1.82; 95% CI, 1.37-2.40; $P < .001$), and >2 procedures by almost 3-fold (aOR, 2.83; 95% CI, 2.07-3.85; $P < .001$). Concomitant tricuspid surgery had no significant difference from isolated MV surgery (aOR, 1.20; 95% CI, 0.84-1.72, $P = .3$). Concomitant left atrial appendage ligation was associated with lower mortality (OR, 1.61; 95% CI, 0.50-1.75; $P < .001$) before adjusting for other variables.

Random forest analysis. Based on a bRF model of 3000 trees—which has an area under the curve of 0.785, a Brier score of 0.044, a sensitivity of 0.761, and a specificity of 0.662 (with the same threshold of 0.049)—the variable importance ranked each variable's impact in classifying the data (Figure 3). Based on variable selection, the most important variables associated with mortality include higher Elixhauser score, end-stage CKD, >2 concomitant procedures, morbid obesity, nonelective admission, advanced age, mitral valve repair, and no atrial fibrillation.

For preoperative factors, the most important complex interactions with the Elixhauser score included age, year of surgery, atrial fibrillation, female sex, dyslipidemia, and coronary artery disease. Morbid obesity, female sex, and end-stage CKD had common interactions

TABLE 3. Univariable (unadjusted) and multivariable (adjusted) logistic regression models

Characteristic	Univariable module			Multivariable module		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age group (y)				–	–	–
50-64	–	–		–	–	–
18-49	0.66	0.47-0.92	**.014**	–	–	–
65-79	1.27	1.04-1.55	**.017**	–	–	–
80+	1.32	0.84-2.07	.2	–	–	–
Age (*z* score)*	1.24	1.13-1.37	**<.001**	1.24	1.08-1.43	**.002**
Female Sex	1.24	1.03-1.49	**.026**	1.08	0.87-1.33	.5
Race (Ref: Non-Hispanic White)						
Black	0.91	0.69-1.20	.5	0.84	0.62-1.15	.3
Hispanic	0.87	0.60-1.27	.5	0.75	0.50-1.12	.2
Year (*z* score)*	0.90	0.82-0.99	**.027**	0.93	0.82-1.06	.3
Insurance (Ref: non-insured/Medicaid)						
Medicare	1.88	1.55-2.27	**<.001**	0.98	0.70-1.35	.9
Private	0.46	0.36-0.58	**<.001**	0.69	0.49-0.97	**.033**
Income 150% FPL	0.70	0.54-0.91	**.007**	0.75	0.57-0.99	**.041**
Elixhauser (*z* score)*	2.40	2.18-2.64	**<.001**	2.10	1.87-2.36	**<.001**
BMI >40	2.31	1.92-2.78	**<.001**	1.80	1.46-2.22	**<.001**
HTN	0.58	0.48-0.70	**<.001**	0.91	0.73-1.14	.4
DM - no chronic complications	1.31	1.08-1.59	**.006**	1.32	1.05-1.66	**.017**
DM - with chronic complications	1.80	1.39-2.32	**<.001**	1.32	0.97-1.81	.081
Previous MI	1.17	0.85-1.63	.3	1.10	0.74-1.63	.6
Dyslipidemia	0.65	0.54-0.78	**<.001**	0.76	0.62-0.94	**.011**
CAD	1.18	0.97-1.42	.092	1.01	0.79-1.30	>.9
PAD	1.63	1.21-2.19	**.001**	1.10	0.79-1.53	.6
COPD	1.17	0.94-1.44	.2	0.75	0.59-0.95	**.016**
Afib	0.61	0.51-0.73	**<.001**	0.44	0.35-0.55	**<.001**
TIA	0.60	0.35-1.03	.063	0.70	0.40-1.26	.2
Ischemic stroke	5.19	2.24-12.0	**<.001**	2.75	0.92-8.24	.072
Nonischemic stroke	1.69	1.25-2.28	**<.001**	0.95	0.68-1.33	.8
End-stage CKD	3.99	2.99-5.32	**<.001**	1.44	1.0-2.09	.053
CHF admission	2.37	1.51-3.71	**<.001**	1.39	0.85-2.27	.2
Redo after valve	1.54	0.97-2.45	.066	1.63	1.01-2.63	**.044**
Redo after CABG	1.47	0.99-2.18	.054	1.36	0.88-2.09	.2
Previous PCI	1.45	1.08-1.96	**.014**	1.41	0.98-2.04	.067
Endocarditis	2.73	2.12-3.51	**<.001**	1.24	0.89-1.72	.2
Mitral regurgitation	0.62	0.51-0.76	**<.001**	0.99	0.79-1.23	.9
Elective admission	0.39	0.33-0.47	**<.001**	0.70	0.56-0.87	**.001**
MV repair (ref: replacement)	0.39	0.31-0.48	**<.001**	0.58	0.46-0.73	**<.001**
Concomitant (ref: Isolated MVR)						
+CABG	1.36	1.07-1.73	**.011**	1.66	1.22-2.25	**.001**
+AVR	1.59	1.26-2.00	**<.001**	1.82	1.37-2.40	**<.001**
+AscendingAo	2.00	0.79-5.05	.14	1.68	0.66-4.28	.3
+TVR	0.94	0.69-1.28	.7	1.20	0.84-1.72	.3
>2 procedures	3.12	2.44-3.98	**<.001**	2.83	2.07-3.85	**<.001**
LAAL/maze	0.61	0.50-0.75	**<.001**	0.92	0.73-1.17	.5

Bold indicates $P < .05$. *OR*, Odds ratio; *FPL*, federal poverty level; *BMI*, body mass index; *HTN*, hypertension; *DM*, diabetes; *MI*, myocardial infarction; *CAD*, coronary artery disease; *PAD*, peripheral arterial disease; *COPD*, chronic obstructive pulmonary disease; *Afib*, atrial fibrillation; *TIA*, transient ischemic attack; *CKD*, chronic kidney disease; *CHF*, congestive heart failure; *Redo*, reoperation after previous CABG or valve surgery; *CABG*, coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *MV*, mitral valve; *AVR*, aortic valve replacement; *AscendingAo*, aortic surgery; *TVR*, tricuspid valve replacement; *LAAL*, left atrial appendage ligation. *z Score transformation= (value−mean)/SD.

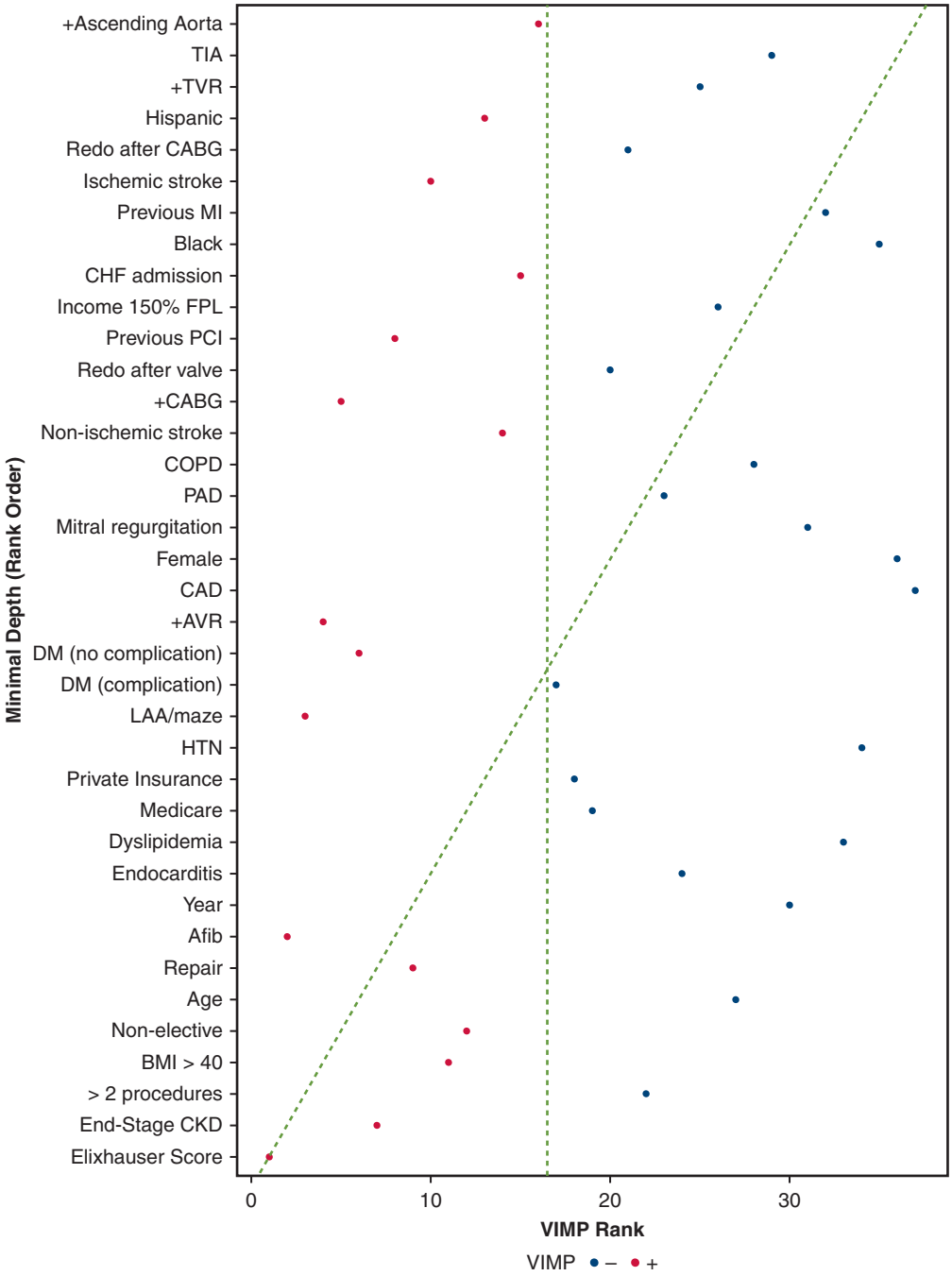


FIGURE 3. Minimal depth and variable importance (*VIMP*) rankings for random forest variables. The top independent variables were ordered according to their minimal depth, where variables with the lowest minimal depth are the most important. *TIA*, Transient ischemic attack; *TVR*, transcatheter valve replacement; *CABG*, coronary artery bypass graft; *MI*, myocardial infarction; *CHF*, congestive heart failure; *FPL*, federal poverty level; *PCI*, percutaneous coronary intervention; *COPD*, chronic obstructive pulmonary disease; *PAD*, peripheral artery disease; *CAD*, coronary artery disease; *AVR*, aortic valve replacement; *DM*, diabetes mellitus; *LAA*, left atrial appendage; *HTN*, hypertension; *Afib*, atrial fibrillation; *BMI*, body mass index; *CKD*, chronic kidney disease.

with the Elixhauser score, age, and year of surgery. Further interactions for female sex included dyslipidemia and coronary artery disease (Figure E2). Partial plots for continuous variables are presented in Figure E3.

Secondary Outcomes

Perioperative complications. The most common complication was bleeding (54%), followed by acute perioperative renal failure (31%). Patients with isolated MV surgery showed lower bleeding (52% vs 57%; $P < .001$) and renal

failure (24% vs 38%; $P < .001$) than patients undergoing concomitant MV surgery. Wound complications were 2-fold higher in patients with morbid obesity (1.4% vs 0.7%; $P = .002$) who also had higher rates of perioperative renal failure (39% vs 26%; $P < .001$). Table 2 summarizes perioperative complications.

Index hospitalization LOS. The median hospital LOS was 9 days (range, 6-15 days). Those with morbid obesity had 2 days higher LOS (11 days [range, 7-19 days] vs 9 days [range, 6-14 days]; $P < .001$). The absence of in-hospital complications was associated with lower LOS by 3 days (7 days [range, 5-10 days] vs 10 days [range, 7-17 days]; $P < .001$) (Figure 4 [left panel]).

Index hospitalization cost. The median cost of hospitalization was $54,572 (range, $39,459-$79,190). There was an increased cost with BMI ≥40 by $8655 (median, $60,742 [range, $43,163-$91,917] vs median, $52,087 [range, $38,279-$73,913]; $P < .001$). The absence of in-hospital complications was associated with lower cost by $18,289 ($41,046 [range, $32,228-$54,134] vs $59,335 [range, $43,338-$86,278]; $P < .001$) (Figure 4 [right panel]).

Discharge disposition. Most patients were discharged home (71% [n = 34,405]). Patients with morbid obesity were less likely to be discharged home than patients with BMI <40 (62% vs 75%; $P < .001$). Table 4 includes the results for hospital LOS, cost, and discharge disposition.

DISCUSSION

Obesity is highly prevalent in cases of MV surgery, with an in-hospital mortality risk of 5.0%. In our nationwide retrospective study representing 48,775 patients, we found that patient demographics and operative characteristics such as Elixhauser score, redo valve surgery, and concomitant surgeries increased the likelihood of in-hospital mortality. However, some comorbidities, such as previous myocardial infarction, coronary artery disease, and peripheral artery disease, did not appear to affect mortality adversely after adjustment for other variables, which indicates the need for further in-depth analysis. Socioeconomic status-related factors, such as income, were associated with increased risk of mortality. Additionally, perioperative complications played an important role in increasing LOS and hospital costs.

Elixhauser Score

Among the most useful instruments for predicting in-hospital mortality was the Elixhauser comorbidity index. This model was designed to estimate the preoperative risk to help providers make optimal care and management decisions for patients. This instrument can also help with patient autonomy and decision making around procedures because it can offer survival and risk predictions. Estimations are based on 31 ICD-coded comorbidities and have been shown to be an accurate predictor of mortality in multiple surgical settings, including cardiac surgery.[15] When predicting mortality, this instrument was found to be superior to individual comorbidities,[16] and it has improved our model's performance without causing multicollinearity (Table E2). In our study, an increased Elixhauser score was associated with higher in-hospital mortality, and it was the single most important preoperative variable. The literature indicates similar trends of lower survival rates in patients with more comorbidities, especially in older individuals.[17,18]

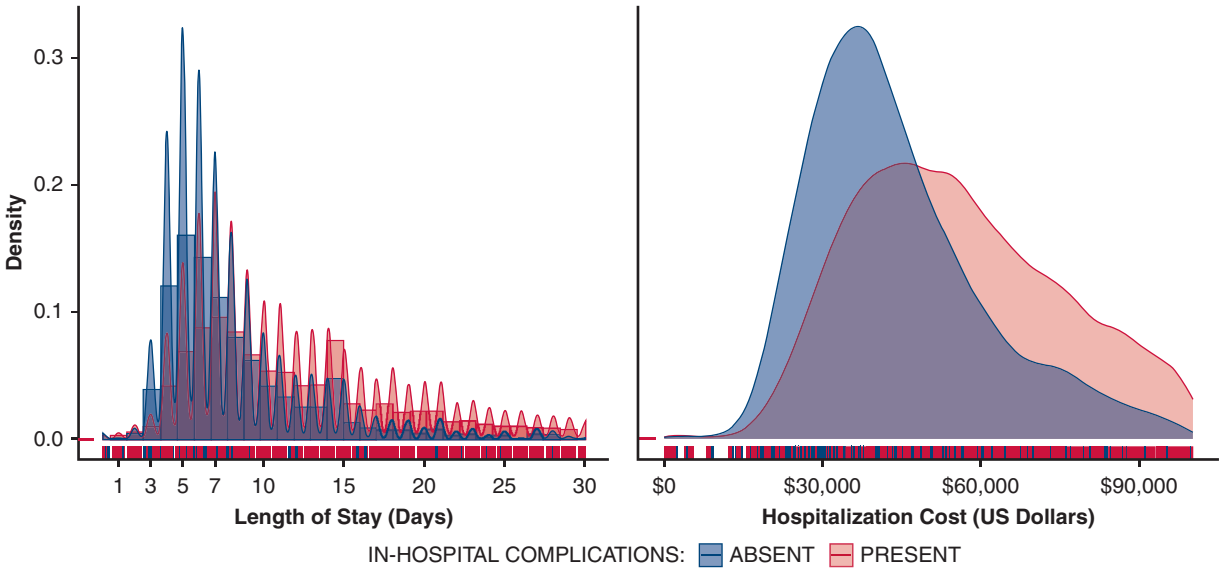


FIGURE 4. Density distributions in patients with absent and present complications in terms of hospital length of stay and hospitalization cost.

TABLE 4. In-hospital length of stay, cost, and discharge disposition

Characteristic	Patients with obesity				Patients with complications		
	Overall (n = 48,775)	BMI 30-39 (n = 32,430)	BMI ≥40 (n = 16,345)	*P* value*	No (n = 10,575)	Yes (n = 38,200)	*P* value*
Length of stay	9 (6-15)	9 (6-14)	11 (7-19)	**<.001**	7 (5-10)	10 (7-17)	**<.001**
Length of stay >10 d	21,415 (44)	12,620 (39)	8795 (54)	**<.001**	2325 (22)	19,090 (50)	**<.001**
Cost ($)	54,572 (39,459-79,190)	52,087 (38,279-73,913)	60,742 (43,163-91,917)	**<.001**	41,046 (32,228-54,134)	59,335 (43,338-86,278)	**<.001**
Unknown	595	430	165		60	535	
Disposition				**<.001**			**<.001**
No transfer	34,405 (71)	24,250 (75)	10,155 (62)		8805 (83)	25,600 (67)	
Transfer to acute care	480 (1.0)	235 (0.7)	245 (1.5)		40 (0.4)	440 (1.2)	
Transfer to other facility	13,870 (28)	7935 (24)	5935 (36)		1725 (16)	12,145 (32)	
Unknown	20	10	10		5	15	

Values are presented as median (interquartile range) or n (%). Bold indicates $P < .05$. *BMI*, Body mass index. *Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao and Scott second-order correction.

The effect of the Elixhauser score on in-hospital mortality can potentially inform trends in surgery characteristics. We found that cases of concomitant MV surgery with other valve surgeries were associated with increased mortality. Patients only in need of isolated procedures may indicate a lower valvular disease-related risk profile. Across multiple surgical specialties, it is commonly reported that urgent operations carry a risk of higher morbidity and mortality rates.[19] We found a significant protective effect of elective surgery in our study. Both of these surgical characteristics—single, elective procedures—may suggest that patients with better outcomes had a preoperative environment that allows better health education and clinician workup of individual risk factors. Furthermore, MV repair was associated with a 42% lower risk of mortality than replacement. Therefore, knowledge of in-hospital mortality predictors can allow providers to better personalize preventive measures and allow for better hospitalization course with efficient health care resource utilization.

Sex Disparities

Sex differences in mortality have been previously reported in MV surgery, including in the setting of female patients with obesity.[20] We found a significant risk for females in our unadjusted model, and multiple interactions by the multivariable random forest analysis, supporting the data suggesting that increased mortality among women is multifactorial. One common explanation for this trend is that women receiving treatment are typically older. Although age is an important risk factor, studies that have stratified the effect of sex by age indicate that worse prognosis by sex is a factor even for women younger than age 50 years.[21] These findings can be attributed to the higher risk profiles carried in these patients, holding a greater number of comorbidities. Additional studies looking into sex-based differences in cardiac surgery outcomes found women of all ages to have higher rates of comorbidities,[22] possibly aligning with our study's finding that a higher Elixhauser score correlates to a greater mortality risk with important interaction with sex. Though the characteristics of female patients play an important role in outcomes, female sex was also found to be independently associated with mortality when adjusted for comorbidities.[23] Because there is a greater prevalence of obesity among women than men,[24] and women often have worse MV diseases,[25] we found a complex interaction among women by overall comorbidity, age, and year of surgery. We also find an interaction and correlation indication with chronic coronary artery disease and dyslipidemia, as well as mitral regurgitation. Additional interactions include obstructive pulmonary disease and diabetes. Thus, awareness of the greater risk in female patients before and during hospitalization may allow for better outcomes and optimal care. Further research is required to understand the coronary artery disease burden in women with obesity undergoing MV surgery and the role of concomitant CABG at such presentation.

Socioeconomic Disparities

Socioeconomic status is a well-studied factor in individual health outcomes. A previous study found that patients with lower socioeconomic status had higher mortality rates, including those patients undergoing MV surgery.[26] This difference in outcomes is also multifactorial. Patients of lower socioeconomic status often have more comorbidities (eg, dyslipidemia, coronary artery disease, and atherosclerotic disease). In addition, women tend to be poorer than men, and as previously described, female sex is associated with mortality. Another study showed that lower socioeconomic status was associated with reduced survival, even when adjusted for race.[27] Similarly, in our study, we found in our unadjusted analysis that income 150% above the federal poverty level—suggesting higher socioeconomic status—was associated with lower mortality. Furthermore, the type

of insurance may be influenced by individual patient's socioeconomic status, which also appeared to affect mortality.

Hospitalization Course, Cost, and LOS

Among the factors that may decrease adverse outcomes in this population is using less-invasive approaches when valvular surgeries are performed.[28] The minimally invasive right-thoracotomy valve surgery, pioneered in part by this article's senior author (J.L.), results in lower mortality and morbidity (in the form of incidence of acute renal failure, prolonged intubation, reintubation, and deep wound infections) than the standard median sternotomy approach.[29] Furthermore, minimally invasive approaches reduce, if not eliminate, wound complications. A previous study in this journal indicated that a BMI increase of 5 points leads to a 38% increase in the risk of wound infection.[6] We noticed in our findings a trend for wound complications in patients with morbid obesity. Overall, it is clear that reducing complications significantly reduces hospitalization LOS and cost. Our findings indicate that patients who experience no complications during their hospitalization for MV surgery use fewer resources, resulting in a cost reduction by a median of $18,313 and faster discharge; thus, it is no surprise that minithoracotomy MV surgery could lead to better outcomes and quality metrics.

The Role of Machine Learning

Our study indicates that—using traditional statistical models—mortality risk will trend in certain directions for specific predictors but disappear when the models are adjusted, as in the case where renal failure and CHF admission. Although it is interesting that the obesity paradox was explained in the context of preexisting cardiac diseases that include hypertension,[30] atrial fibrillation,[31] CHF,[32] and CKD,[33] our data are inconclusive and further analysis with patients undergoing MV surgery of different BMI categories is still warranted. Our in-depth analysis—using advanced machine learning algorithms—shed light on some complex inherent interactions of the previous factors. For example, female sex (along with dyslipidemia, coronary artery disease, and chronic obstructive pulmonary disease) was a common variable of interaction for CHF admission and end-stage CKD. In addition to supporting sex disparities evidence and delayed care of female patients, this raises a question on how to treat female patients with CHF or CKD, and the role of their multiple comorbidities. Thus, a better understanding of multiple elements involved in MV surgery patient care before and during admission for those with obesity is necessary because that may lead to lower complications and decreased mortality. Software tools to explore these interactions are being actively developed. These techniques (ie, break-down plots, Shapley Additive Explanations, and Ceteris-paribus methods) that complement the overall variable importance metrics discussed here, describe the influence of interactions on individuals in a dataset.[34]

Limitations

The HCUP-NIS is a retrospective database of discharge records, making it susceptible to errors in ICD coding. The possibility of selection bias and the lack of data granularity, due to the administrative nature of this database, could have impacted bRF predictability; furthermore, the currently available software for random forest methodology does not support the recently developed sample-selection-adjusted models.[35] Inconsistent coding practices among institutions may have resulted in over- or underestimations of events, although robust quality control measures were in place to minimize these discrepancies. In our assessment of the secondary end points, some ICD codes were not helpful to distinguish between comorbidities and complications; thus, the rate of complications is likely to be overestimated given the existing limitations of the administrative databases. In addition, the lack of data granularity and long-term follow-up information does not allow us to assess dynamic changes in obesity with BMI over time because patients lose/gain weight, but rather the data provide a snapshot of patients' obesity status.

CONCLUSIONS

There is a significant intersection between obesity and MV surgery outcomes. Although patients with obesity may have reasonable outcomes, morbid obesity is often associated with a higher number of comorbidities, leading to a higher risk of complications and mortality.

Understanding the influence of these comorbidities can better educate clinicians on preventive measures. The results of our study align with current literature, indicating worse in-hospital mortality rates in older and female patients with multiple comorbidities; thus, special care should be taken when referring and performing MV surgery on patients with obesity.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

The authors thank April Mann for writing support through the University of Miami CTSI. The authors also thank the reviewers for their helpful comments and recommendations on earlier drafts of this manuscript that improved this work.

References

1. Carbone S, Canada JM, Billingsley HE, Siddiqui MS, Elagizi A, Lavie CJ. Obesity paradox in cardiovascular disease: where do we stand? *Vasc Health Risk Manag*. 2019;15:89-100.
2. Lavie CJ, Arena R, Alpert MA, Milani RV, Ventura HO. Management of cardiovascular diseases in patients with obesity. *Nat Rev Cardiol*. 2018;15:45-56.
3. Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A. Effects of obesity and small body size on operative and long-term outcomes of coronary artery bypass surgery: a propensity-matched analysis. *Ann Thorac Surg*. 2005;79:1976-86.
4. Ghanta RK, LaPar DJ, Zhang Q, Devarkonda V, Isbell JM, Yarboro LT, et al. Obesity increases risk-adjusted morbidity, mortality, and cost following cardiac surgery. *J Am Heart Assoc*. 2017;6(3):e003831.
5. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation*. 2019;139:e56-528.
6. Burns DJP, Rapetto F, Angelini GD, Benedetto U, Caputo M, Ciulli F, et al. Body mass index and early outcomes following mitral valve surgery for degenerative disease. *J Thorac Cardiovasc Surg*. 2021;161:1765-73.e2.
7. Minol JP, Dimitrova V, Petrov G, Langner R, Boeken U, Lichtenberg A, et al. Predictive value of body mass index in minimally invasive mitral valve surgery. *Thorac Cardiovasc Surg*. 2022;70:106-11.
8. Nazir S, Ahuja KR, Macciocca M, Changal K, Oostra C, Mangi MA, et al. Association of body mass index with outcomes in patients undergoing transcatheter mitral valve repair. *Am J Cardiol*. 2020;134:158-60.
9. HCUP National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2012-2020. Accessed May 11, 2023. www.hcup-us.ahrq.gov/nisoverview.jsp [Note: HCUP Calculating Standard Errors. https://hcup-us.ahrq.gov/tech_assist/standarderrors/508/508course_2016.jsp].
10. Stamou SC, Nussbaum M, Stiegel RM, Reames MK, Skipper ER, Robicsek F, et al. Effect of body mass index on outcomes after cardiac surgery: is there an obesity paradox? *Ann Thorac Surg*. 2011;91:42-7.
11. Sharma A, Vallakati A, Einstein AJ, Lavie CJ, Arbab-Zadeh A, Lopez-Jimenez F, et al. Relationship of body mass index with total mortality, cardiovascular mortality, and myocardial infarction after coronary revascularization: evidence from a meta-analysis. *Mayo Clin Proc*. 2014;89:1080-100.
12. Ishwaran H, O'Brien R. Commentary: the problem of class imbalance in biomedical data. *J Thorac Cardiovasc Surg*. 2021;161:1940-1.
13. Alnajar A, Ibrahim W, Mendoza CE. Are the outcomes of TAVR significantly riskier for solid organ transplant recipients than for the general population? *J Card Surg*. 2022;37:608-9.
14. Alnajar A, Arora Y, Benck KN, Kabir Khan A, Altabbakh O, Dar T, et al. Isolated tricuspid valve repair versus replacement: predictors of mortality on the national level. *Innovations (Phila)*. 2023;18:58-66.
15. Mehta HB, Dimou F, Adhikari D, Tamirisa NP, Sieloff E, Williams TP, et al. Comparison of comorbidity scores in predicting surgical outcomes. *Med Care*. 2016;54:180-7.
16. Potts J, Nagaraja V, Al Suwaidi J, Brugaletta S, Martinez SC, Alraies C, et al. The influence of Elixhauser comorbidity index on percutaneous coronary intervention outcomes. *Catheter Cardiovasc Interv*. 2019;94:195-203.
17. Vassileva CM, Mishkel G, McNeely C, Boley T, Markwell S, Scaife S, et al. Long-term survival of patients undergoing mitral valve repair and replacement: a longitudinal analysis of medicare fee-for-service beneficiaries. *Circulation*. 2013;127:1870-6.
18. Bonnet V, Boisselier C, Saplacan V, Belin A, Gérard JL, Fellahi JL, et al. The role of age and comorbidities in postoperative outcome of mitral valve repair: a propensity-matched study. *Medicine (Baltimore)*. 2016;95:e3938.
19. Mullen MG, Michaels AD, Mehaffey JH, Guidry CA, Turrentine FE, Hedrick TL, et al. Risk associated with complications and mortality after urgent surgery vs elective and emergency surgery: implications for defining "quality" and reporting outcomes for urgent surgery. *JAMA Surg*. 2017;152:768-74.
20. El-Andari R, Bozso SJ, Kang JJH, Boe D, Hong Y, Gill RS, et al. The effects of body mass index on long-term outcomes and cardiac remodeling following mitral valve repair surgery. *Int J Obes*. 2021;45:2679-87.
21. Vaccarino V, Abramson JL, Veledar E, Weintraub WS. Sex differences in hospital mortality after coronary artery bypass surgery: evidence for a higher mortality in younger women. *Circulation*. 2002;105:1176-81.
22. Woods SE, Noble G, Smith JM, Hasselfeld K. The influence of gender in patients undergoing coronary artery bypass graft surgery: an eight-year prospective hospitalized cohort study. *J Am Coll Surg*. 2003;196:428-34.
23. Blankstein R, Ward RP, Arnsdorf M, Jones B, Lou YB, Pine M. Female gender is an independent predictor of operative mortality after coronary artery bypass graft surgery: contemporary analysis of 31 Midwestern hospitals. *Circulation*. 2005;112:I323-7.
24. Cooper AJ, Gupta SR, Moustafa AF, Chao AM. Sex/gender differences in obesity prevalence, comorbidities, and treatment. *Curr Obes Rep*. 2021;10:458-66.
25. Seeburger J, Eifert S, Pfannmuller B, Garbade J, Vollroth M, Misfeld M, et al. Gender differences in mitral valve surgery. *Thorac Cardiovasc Surg*. 2013;61:42-6.
26. Birkmeyer NJ, Gu N, Baser O, Morris AM, Birkmeyer JD. Socioeconomic status and surgical mortality in the elderly. *Med Care*. 2008;46:893-9.
27. Koch CG, Li L, Kaplan GA, Wachterman J, Shishehbor MH, Sabik J, et al. Socioeconomic position, not race, is linked to death after cardiac surgery. *Circ Cardiovasc Qual Outcomes*. 2010;3:267-76.
28. Thourani VH, Keeling WB, Kilgo PD, Puskas JD, Lattouf OM, Chen EP, et al. The impact of body mass index on morbidity and short- and long-term mortality in cardiac valvular surgery. *J Thorac Cardiovasc Surg*. 2011;142:1052-61.
29. Santana O, Reyna J, Grana R, Buendia M, Lamas GA, Lamelas J. Outcomes of minimally invasive valve surgery versus standard sternotomy in obese patients undergoing isolated valve surgery. *Ann Thorac Surg*. 2011;91:406-10.
30. Jayedi A, Shab-Bidar S. Nonlinear dose-response association between body mass index and risk of all-cause and cardiovascular mortality in patients with hypertension: a meta-analysis. *Obes Res Clin Pract*. 2018;12:16-28.
31. Sandhu RK, Ezekowitz J, Andersson U, Alexander JH, Granger CB, Halvorsen S, et al. The 'obesity paradox' in atrial fibrillation: observations from the ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) trial. *Eur Heart J*. 2016;37:2869-78.
32. Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA. Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J*. 2008;156:13-22.
33. Park J, Ahmadi SF, Streja E, Molnar MZ, Flegal KM, Gillen D, et al. Obesity paradox in end-stage kidney disease patients. *Prog Cardiovasc Dis*. 2014;56:415-25.
34. Biecek P, Burzykowski T. *Explanatory Model Analysis: Explore, Explain, and Examine Predictive Models*. CRC Press; 2021.
35. Cook J. Sample-selection-adjusted random forests. *Int J Data Sci Anal*. 2022;14:375-88.

Key Words: adult cardiac, obesity, mitral valve, mortality, machine learning, random forest

E-References

E1. Lumley CT. Survey: Analysis of Complex Survey Samples. R Package Version 4.0. Accessed July 1, 2023. https://cran.r-project.org/package=survey

E2. Gasparini A. Comorbidity: an R package for computing comorbidity scores. *J Open Source Softw.* 2018;3:648.

E3. Mayer M. missRanger: fast imputation of missing values. R package version 2.1.3; 2021. https://CRAN.R-project.org/package=missRanger

E4. Ishwaran H, Lu M, Kogalur UB. randomForestSRC: getting started with randomForestSRC vignette; 2021. http://randomforestsrc.org/articles/getstarted.html

E5. Ishwaran H, Lu M, Kogalur UB. randomForestSRC: variable importance (VIMP) with subsampling inference vignette; 2021. http://randomforestsrc.org/articles/vimp.html

E6. Ishwaran H, Chen X, Minn AJ, Lu M, Lauer MS, Kogalur UB. randomForestSRC: minimal depth vignette; 2021. http://randomforestsrc.org/articles/minidep.html

E7. Ehrlinger J. ggRandomForests: visually exploring random forests. R package version 2.2.0; 2020. https://cran.r-project.org/package=ggRandomForests

E8. Sjoberg DD, Whiting K, Curry M, Lavery JA, Larmarange J. Reproducible summary tables with the gtsummary package. *R J.* 2021;13:570-80. https://doi.org/10.32614/RJ-2021-053

E9. Gohel D. flextable: functions for tabular reporting. R package version 0.7.2; 2022. https://CRAN.R-project.org/package=flextable

E10. Gohel D. officer: manipulation of microsoft word and powerpoint documents. R package version 0.4.3; 2022. https://CRAN.R-project.org/package=officer

E11. Klik M. fst: lightning fast serialization of data frames. R package version 0.9.8; 2020. https://CRAN.R-project.org/package=fst

E12. Wickham H, Averick M, Bryan J, Chang W, McGowan L, François R, et al. Welcome to the tidyverse. *J Open Source Softw.* 2019;4:1686. https://doi.org/10.21105/joss.01686

E13. Wilke C. cowplot: streamlined plot theme and plot annotations for 'ggplot2'. R package version 1.1.1; 2020. https://CRAN.R-project.org/package=cowplot

E14. Harrell FE Jr. rms: regression modeling strategies. R package version 6.3-0; 2022. https://CRAN.R-project.org/package=rms

E15. Signorell A, Aho K, Alfons A, Anderegg N, Aragon T, Arachchige C, et al. DescTools: tools for descriptive statistics. R package version 0.99.45; 2022. https://cran.r-project.org/package=DescTools

E16. Cui B. DataExplorer: automate data exploration and treatment. R package version 0.8.2; 2020. https://CRAN.R-project.org/package=DataExplorer

E17. Waring E, Quinn M, McNamara A, Arino de la Rubia E, Zhu H, Lowndes J, et al. Compact and flexible summaries of data. R package version 2.1.5; 2022. https://CRAN.R-project.org/package=skimr

E18. Yoshida K, Bartel A. tableone: create 'Table 1' to describe baseline characteristics with or without propensity score weights. R package version 0.13.2; 2022. https://CRAN.R-project.org/package=tableone

E19. Corporation M, Weston S. doParallel: for each parallel adaptor for the 'parallel' package. R package version 1.0.17; 2022. https://CRAN.R-project.org/package=doParallel

E20. Rinker TW, Kurkiewicz D. pacman: package management for R. version 0.5.0; 2017. http://github.com/trinker/pacman

E21. R Core Team. *R: A Language and Environment For Statistical Computing*. R Foundation for Statistical Computing; 2022.

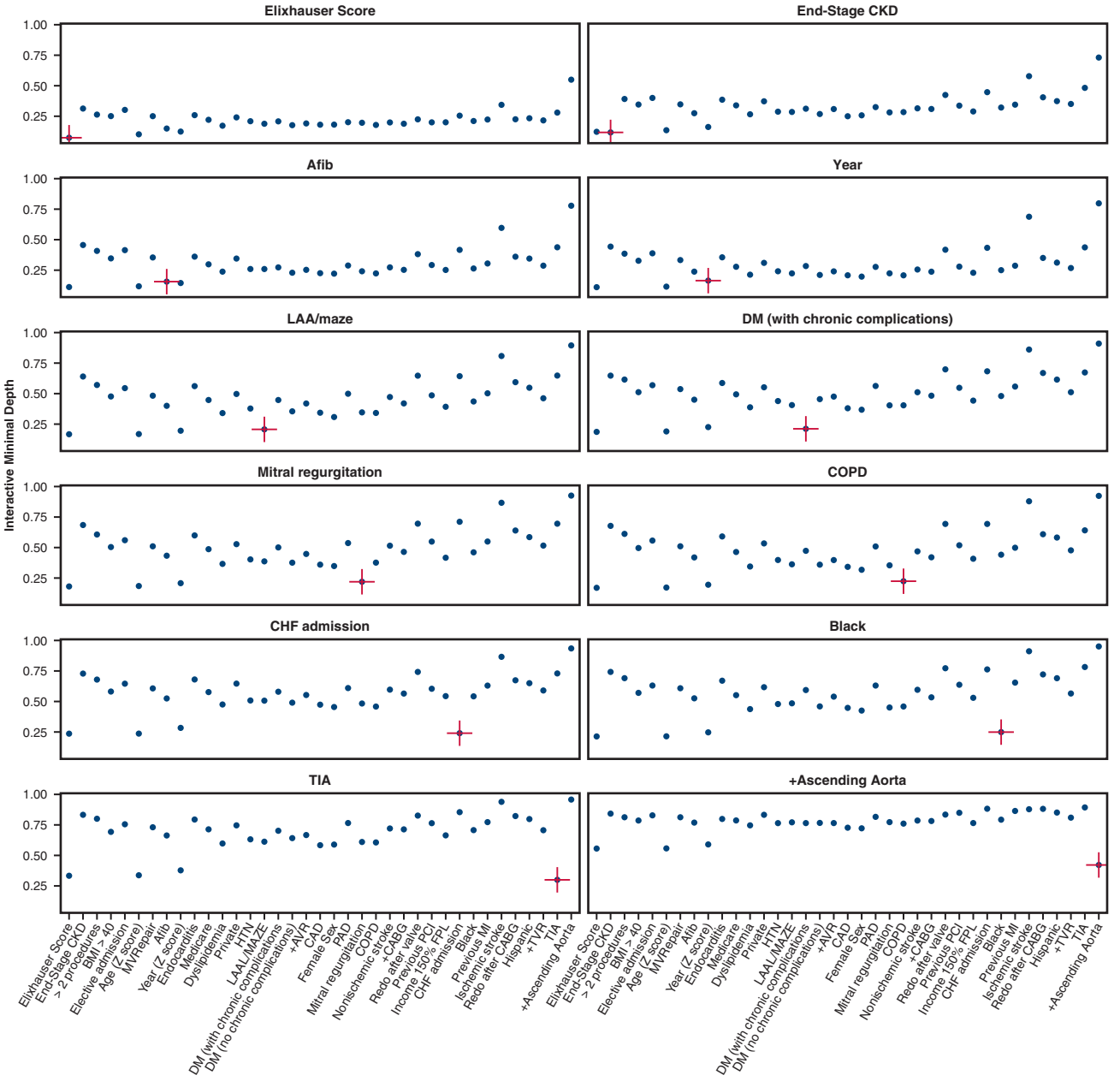


FIGURE E1. Random forest interactions among a few important preoperative variables associated with in-hospital mortality. Variables with the lowest minimal depth denote strong interactions. *CKD*, Chronic kidney disease; *BMI*, body mass index; *MV*, mitral valve; *Afib*, atrial fibrillation; *HTN*, hypertension; *LAAL*, left atrial appendage ligation; *DM*, diabetes mellitus; *AVR*, aortic valve replacement; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *COPD*, chronic obstructive pulmonary disease; *CABG*, coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *FPL*, federal poverty level; *CHF*, congestive heart failure; *MI*, myocardial infarction; *TVR*, transcatheter valve replacement; *TIA*, transient ischemic attack.

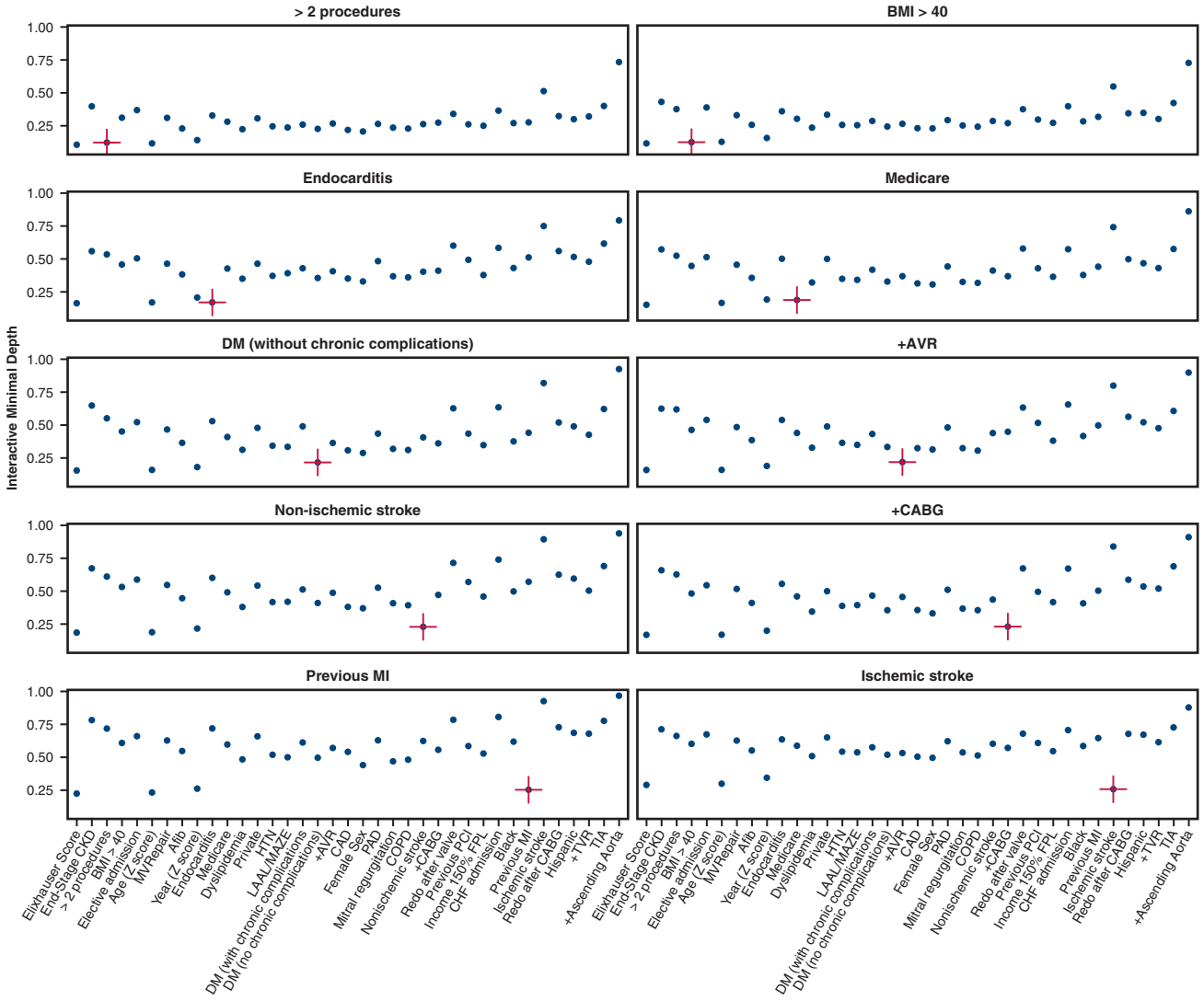


FIGURE E1. Continued.

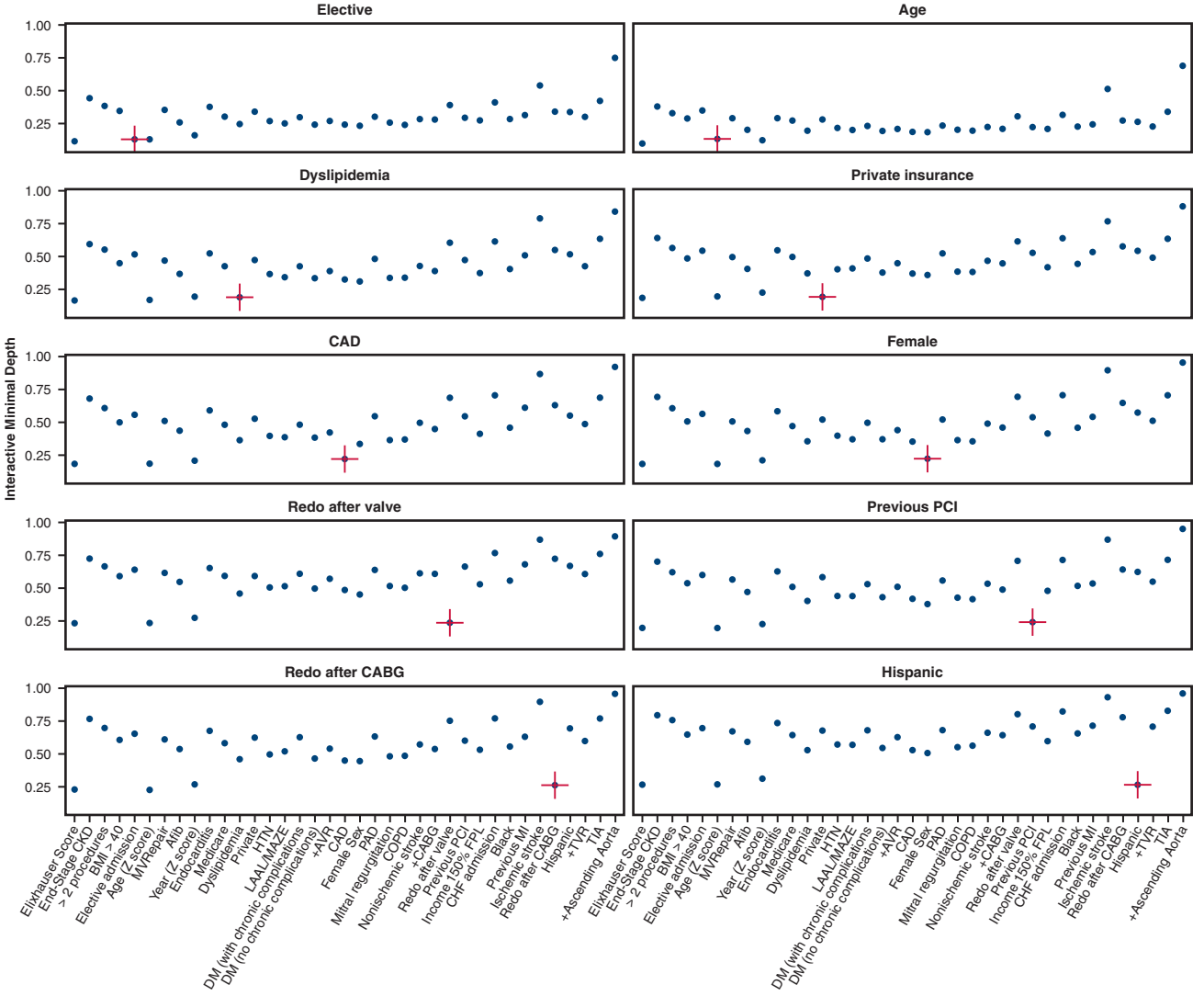


FIGURE E1. Continued.

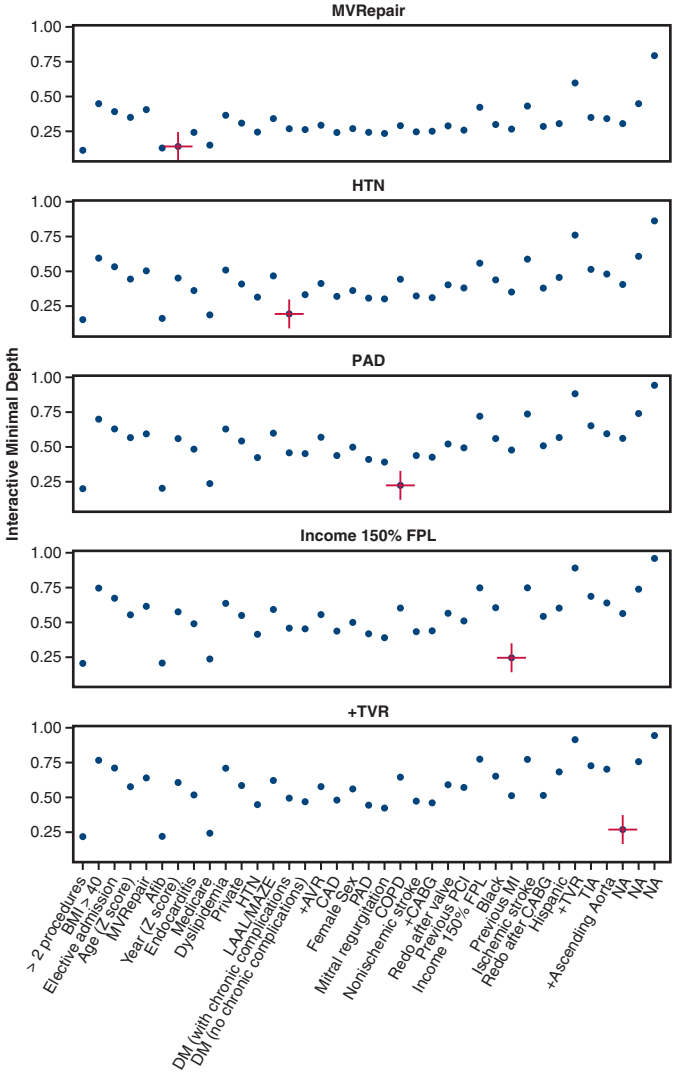


FIGURE E1. Continued.

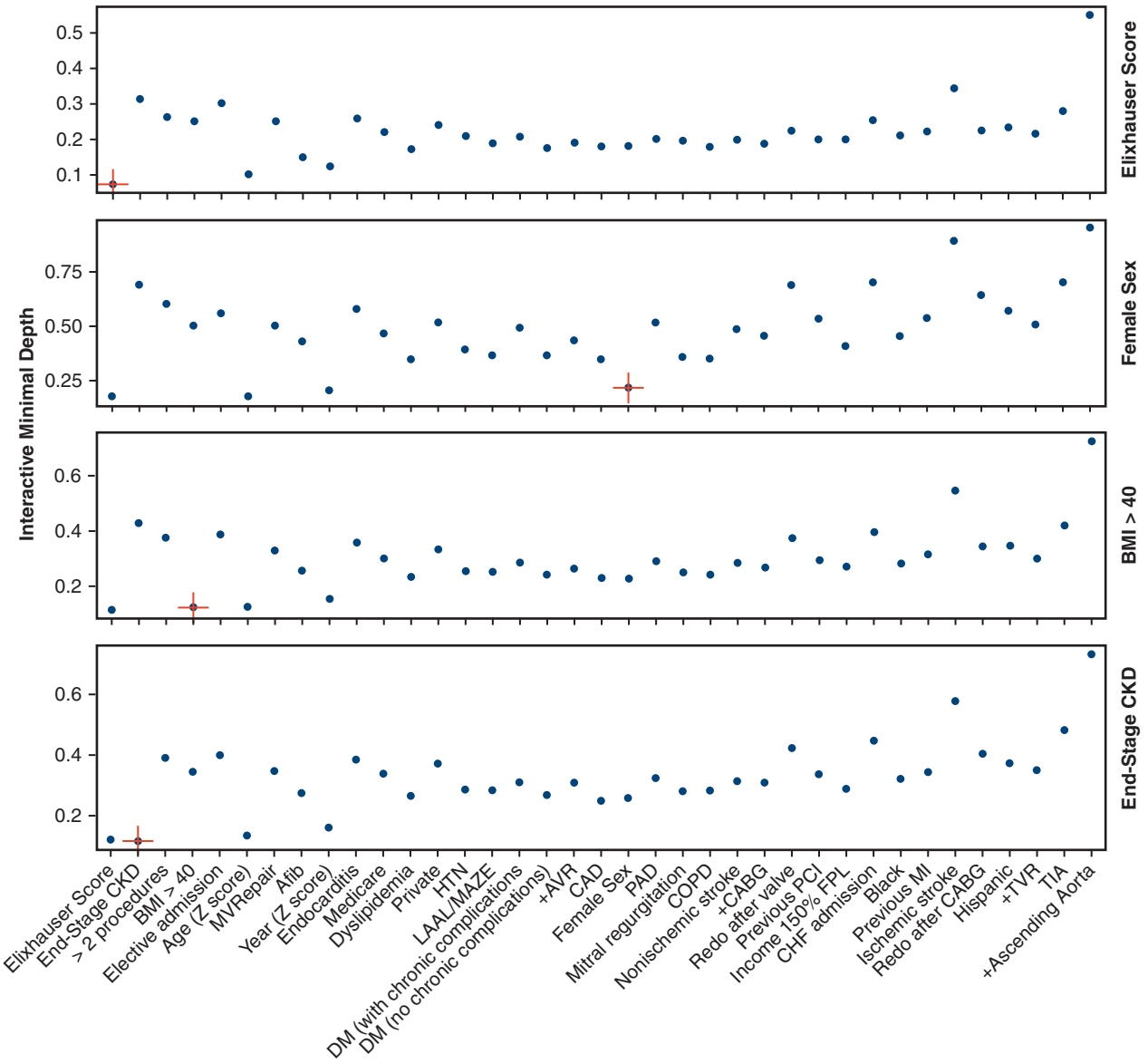


FIGURE E2. Pairwise interactions between all variables. *CKD*, Chronic kidney disease; *BMI*, body mass index; *Afib*, atrial fibrillation; *MV*, mitral valve; *HTN*, hypertension; *LAAL*, left atrial appendage ligation; *DM*, diabetes mellitus; *AVR*, aortic valve replacement; *CAD*, coronary artery disease; *PAD*, peripheral artery disease; *COPD*, chronic obstructive pulmonary disease; *CABG*, coronary artery bypass grafting; *PCI*, percutaneous coronary intervention; *FPL*, federal poverty level; *CHF*, congestive heart failure; *MI*, myocardial infarction; *TVR*, transcatheter valve replacement; *TIA*, transient ischemic attack; *NA*, not available.

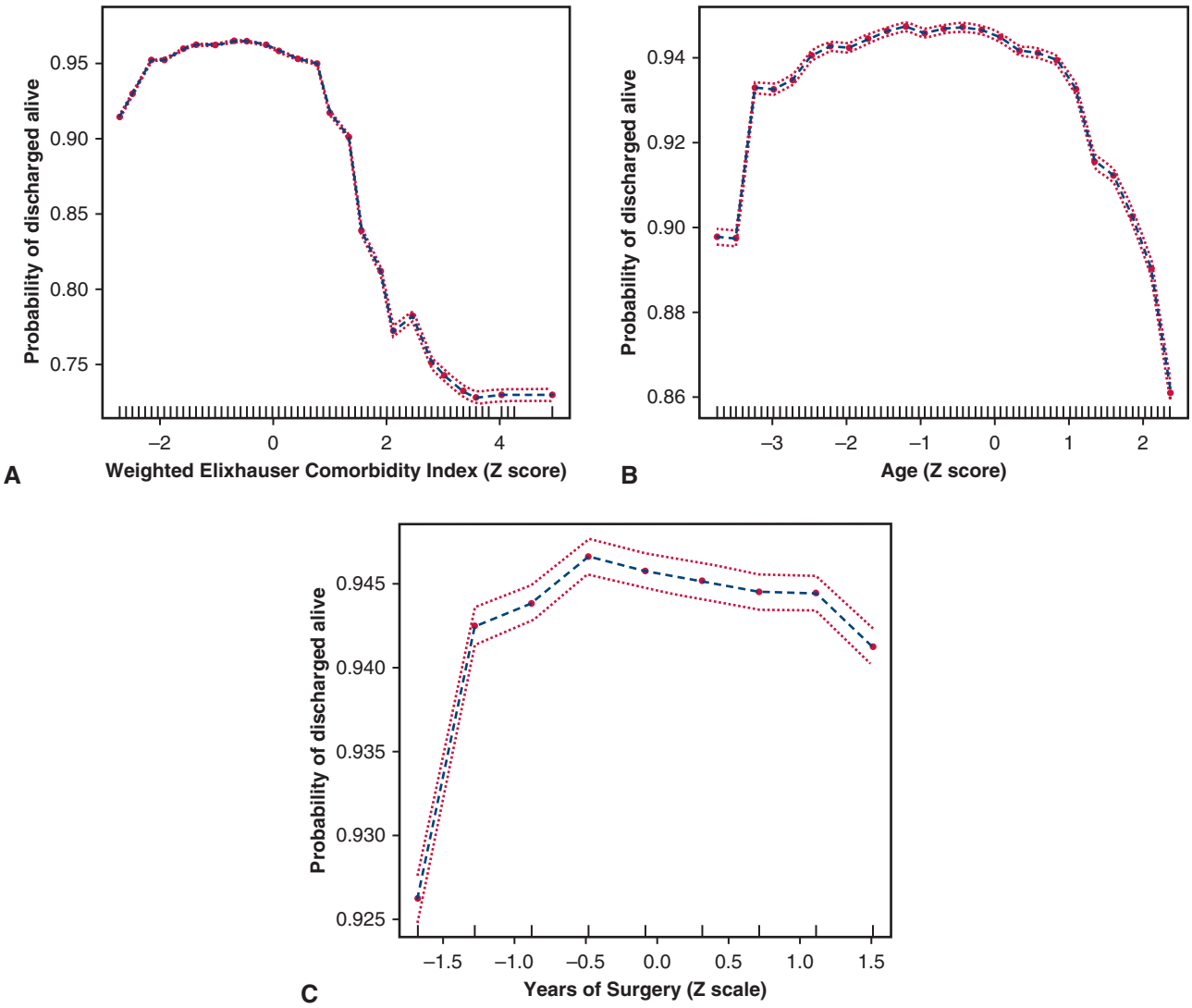


FIGURE E3. Partial plots for (A) age (z score), (B) Elixhauser (z score), and (C) surgical years (z score). The vertical axis displays the ensemble predicted value, whereas $\times$ variables are plotted on the horizontal axis as *red points* and *blue dashed line* for the partial values and *dashed red lines* to indicate a smoothed error bar of ± 2 SE.

TABLE E1. International Classification of Diseases Ninth edition (ICD-9) and ICD Tenth edition (ICD-10) codes

	Diagnostic ICD code
Obesity	
Obesity (BMI >30)	ICD-9: V85.30-V85.39
	ICD-10: Z68.30-Z68.39, E669
Obesity (BMI >40)	ICD-9: V85.4-V85.49, 278.01
	ICD-10: Z68.41-Z68.45, E6601, E662
Obesity (nonspecific: considered as 30-40)	ICD-9: 278.00, 278.02, 278.03
	ICD-10: E66.0-E66.9
Covariate	
Hypertension	ICD-9: 401.1, 401.9, 402.0, 402.1, 402.9, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99
	ICD-10: I10, I11.0, I11.9, I13.0-I13.2, I15.0, I15.1, I15.2, I15.8, I15.9, I16.0, I16.1, I16.9
Diabetes	ICD-9: 249.0, 250.0
	ICD-10: E10.9, E11.0, E11.9, E13.0, E13.1, E13.9, E14.1, E14.9
Diabetes mellitus with chronic complications	ICD-9: 250.40-250.70
	ICD-10: E10.2-E10.5, E11.2-E11.5, E12.2-E12.5, E13.2-E13.5, E14.2-E14.5
Dyslipidemia	ICD-9: 272.0, 272.1, 272.2, 272.4
	ICD-10: E78.0, E78.1, E78.2, E78.4, E78.5, E78.00, E78.01
MI	ICD-9: 412
	ICD-10: I25.2
Coronary artery disease	ICD-9: 412, 414.8, 414.9, 440, 440.1, V12.53
	ICD-10: I20.0, I24.1, I25.1-I25.9, I70.0, I70.1, Z86.74
Peripheral arterial disease	ICD-9: 440.2-440.4, 440.8, 440.9, 443.1-443.9, 447.1, 557
	ICD-10: I70.2-I70.9, I70.20, I70.21, I73.1, I73.8, I73.9, I77.1, I79.0, I79.1, I79.8, K55.1, K55.8, K55.9, Z95.8, Z95.9
Chronic obstructive pulmonary disease	ICD-9: 491.0-491.2, 491.8, 491.9, 492.0, 492.8, 493.02, 493.2, 496
	ICD-10: J40, J41, J42, J43, J44, J47
Atrial fibrillation	ICD-9: 427.31
	ICD-10: I48.0-I48.2, I48.9, I48.11, I48.19, I48.20, I48.21, I48.91
Transient ischemic attack	ICD-9: 435.8, 435.9
	ICD-10: Z86.73, G45.3, G45.8, G45.9
Stroke	ICD-9: 430, 431, 432.0, 432.1, 433.0-433.3, 433.8, 433.9, 434.00, 434.01, 434,10, 434.90, 434.91, 435.0, 435.1, 435.3, 435.9, 435.9, 438.0-438.9
	ICD-10: I60.0-I60.9, I61.0-I61.6, I61.8, I61.9, I62.0, I62.00, I62.01, I62.02, I62.03, I62.1, I62.9, I69.0-I69.2, I63.0-I63.6, I63.8, I63.9, I65.0-I65.2, I65.8, I65.9, I65.01- I65.03, I65.09, I65.21- I65.23, I65.29, I66.0-I66.3, I66.8, I66.9, I66.01- I66.03, I66.09, I66.1, I66.2, I66.8, I66.9, I69.3, I69.8
Chronic kidney disease	ICD-9: 403.01, 403.11, 403.91, 404.01, 404.02, 404.03, 404.11, 404.12, 404.13, 404.91, 404.92, 404.93, 582.0-582.2, 582.4, 582.8, 582.9, 585.1-585.6, 585.9, 586, 588.0, V42.0, V45.1
	ICD-10: I12.0, I12.9, I13.0, I13.1, I13.2, N03.0-N03.4, N03.6-N03.9, N05.0-N05.4, N05.6-N05.9, N18.1-N18.4, N18.6, N18.9, N19, N25.0, O10.2, O10.3, Z49.0-Z49.2, Z94.0, Z99.2
End-stage kidney disease	ICD-9: 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.91, 404.92, 404.93, 585.5-585.6, V42.0, V45.1, V56
	ICD-10: I12.0, I13.2, N18.5-N18.6, Z49.0-Z49.2, Z94.0, Z99.2
Admission for congestive heart failure	ICD-9 (DX1): 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13,404.91, 404.93, 428.0, 428.1-428.9
	ICD-10 (I10_DX1): I09.81, I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5-I42.9, I43, I50.1-I50.4, I50.8, I50.9
Infective endocarditis	ICD-9: 036.42, 074.22, 093.20, 093.21, 093.22, 093.23, 093.24, 098.84, 112.81, 115.04, 115.14, 115.94, 391.1, 397.1, 421.0, 421.1, 421.9, 424.3, 424.90, 424.91, 424.99, 710.0
	ICD-10: I33.0, I33.9, I38, I39, B37.6, B33.21
Prior CABG	ICD-9: V45.81
	ICD-10: Z95.1
Prior valve	ICD-9: V433
	ICD-10: Z95.2, Z95.3, Z95.4
Prior PCI	ICD-9: V45.82
	ICD-10: Z95.5, Z98.61

(Continued)

TABLE E1. Continued

	Diagnostic ICD code
Mitral regurgitation	ICD-9: 396.2, 396.3, 394.1 ICD-10: I34.0, I34.1, Q23.3, I05.1
Postoperative outcomes	
Sternal wound complications	ICD-9: 875, 9983, 99,859 ICD-10: T813, T8141, T8142
Complications due to prosthetic device, implant, or graft	ICD-9: 996.0, 996.1 ICD-10: T82.1- T82.9, T82.01, T82.02
Bleeding	ICD-9: 99.01, 99.04, 997.02, 429.89, 459, 285.1, 286.59, 998.11, 998.12, 998.13, 999.80, 999.83, 999.84, 999.85, 999.88, 999.89 ICD-10: I97.61, I97.410, I97.411, I97.418, I97.42, I97.611, I97.618, R58, D62, D68.311, D68.318, K92.0, R04.0, K92.1, K62.5, K92.2, I51.3, R04.2, R04.9, D50.0
Complete heart block	ICD-9: 426.0, 426.10, 426.11, 426.12, 426.13 ICD-10: I44.0, I44.1, I44.2, I44.30, I44.39
Cardiac arrest	ICD-9: 427.5, 429.4 ICD-10: I46.2, I46.9, I97.1
Stroke	ICD-9: 997.02, 436 ICD-10: I97.810, I97.811, I97.820, I97.821
Acute MI perioperatively	ICD-9: 410 ICD-10: I21
Acute renal injury/failure	ICD-9: 583.6, 583.7, 584.5, 584.8, 584.9 ICD-10: N17.0, N17.1, N17.2, N17.8, N17.9, N19, S37.0
	Procedure ICD codes
Cardiac surgeries	
Mitral valve replacement - open	ICD-9: 35.23, 35.24 ICD-10: 02RG07Z, 02RG08Z, 02RG0JZ, 02RG0KZ
Mitral valve repair - open	ICD-9: 35.12, 35.31, 35.32 ICD-10: 02QG0ZE, 02QG0ZZ, 02UG07E, 02UG07Z, 02UG08E, 02UG08Z, 02UG0JE, 02UG0JZ, 02UG0KE, 02UG0KZ, 027G04Z, 027G0DZ, 027G0ZZ, 02NG0ZZ, 02VG0ZZ, 028D0ZZ, 02QD0ZZ, 02890ZZ, 02Q90ZZ
CABG	ICD-9: 36.10-36.19, 36.2, 36.31, 36.32, 36.39 ICD-10: 02130KW, 02130Z3, 02130Z8, 02130Z9, 02130ZC, 02130ZF, 02130K8, 02130K9, 02130KC, 02130KF, 02130A9, 02130AC, 02130AF, 02130AW, 02130J3, 02130J8, 02130J9, 02130JC, 02130JF, 02130JW, 02130K3, 02120Z8, 02120Z9, 02120ZC, 02120ZF, 0213093, 0213098, 0213099, 021309C, 021309F, 021309W, 02130A3, 02130A8, 02120AW, 02120J3, 02120J8, 02120J9, 02120JC, 02120JF, 02120JW, 02120K3, 02120K8, 02120K9, 02120KC, 02120KF, 02120KW, 02120Z3, 02110Z9, 02110ZC, 02110ZF, 0212093, 0212098, 0212099, 021209C, 021209F, 021209W, 02120A3, 02120A8, 02120A9, 02120AC, 02120AF, 02110J3, 02110J8, 02110J9, 02110JC, 02110JF, 02110JW, 02110K3, 02110K8, 02110K9, 02110KC, 02110KF, 02110KW, 02110Z3, 02110Z8, 02100ZC, 02100ZF, 0211093, 0211098, 0211099, 021109C, 021109F, 021109W, 02110A3, 02110A8, 02110A9, 02110AC, 02110AF, 02110AW, 02100J3, 02100K9, 02100KC, 02100KF, 02100KW, 02100Z3, 02100Z8, 02100Z9, 0210093, 0210099, 021009C, 021009F, 021009W, 02100A3, 02100A8, 02100A9, 02100AC, 02100AF, 02100AW, 0210098, 02100J8, 02100J9, 02100JC, 02100JF, 02100JW, 02100K3, 02100K8, 0210493, 0210498, 0210499, 021049C, 021049F, 021049W, 02104A3, 02104A8, 02104A9, 02104AC, 02104AF, 02104AW, 02104J3, 02104J8, 02104J9, 02104JC, 02104JF, 02104JW, 02104K3, 02104K8, 02104K9, 02104KC, 02104KF, 02104KW, 02104Z3, 02104Z8, 02104Z9, 02104ZC, 02104ZF, 0211493, 0211498, 0211499, 021149C, 021149F, 021149W, 02114A3, 02114A8, 02114A9, 02114AC, 02114AF, 02114AW, 02114J3, 02114J8, 02114J9, 02114JC, 02114JF, 02114JW, 02114K3, 02114K8, 02114K9, 02114KC, 02114KF, 02114KW, 02114Z3, 02114Z8, 02114Z9, 02114ZC, 02114ZF, 0212493, 0212498, 0212499, 021249C, 021249F, 021249W, 02124A3, 02124A8, 02124A9, 02124AC, 02124AF, 02124AW, 02124J3, 02124J8, 02124J9, 02124JC, 02124JF, 02124JW, 02124K3, 02124K8, 02124K9, 02124KC, 02124KF, 02124KW, 02124Z3, 02124Z8, 02124Z9, 02124ZC, 02124ZF, 0213493, 0213498, 0213499, 021349C, 021349F, 021349W, 02134A3, 02134A8, 02134A9, 02134AC, 02134AF, 02134AW, 02134J3, 02134J8, 02134J9, 02134JC, 02134JF, 02134JW, 02134K3, 02134K8, 02134K9, 02134KC, 02134KF, 02134KW, 02134Z3, 02134Z8, 02134Z9, 02134ZC, 02134ZF

(Continued)

TABLE E1. Continued

	Procedure ICD codes
Aortic valve – surgical replacement	ICD-9: 35.20, 35.21, 35.22
	ICD-10: 02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ, 02RF4JZ, 02RF47Z, 02RF48Z, 02RF4KZ, X2RF032
Aortic valve - TAVR	ICD-9: 35.05, 35.06
	ICD-10: 02RF37Z, 02RF38Z, 02RF3JZ, 02RF3KZ, 02RF37H, 02RF38H, 02RF3JH, 02RF3KH
Aorta - open repair or replacement of ascending thoracic aorta	ICD-9: 38.45, 39.52
	ICD-10: 02RX07Z, 02RX08Z, 02RX0JZ, 02RX0KZ, 02QX0ZZ
Tricuspid valve surgery	ICD-9: 35.27, 35.28, 35.14
	ICD-10: 02RJ07Z, 02RJ08Z, 02RJ0JZ, 02RJ0KZ, 02QJ0ZG, 02QJ0ZZ, 027J04Z, 027J0DZ, 027J0ZZ, 02NJ0ZZ, 02UJ07Z, 02UJ08Z, 02UJ0JZ, 02UJ0KZ
LAAL procedure	ICD-9: 37.36
	ICD-10: 02570ZZ, 02B70ZZ, 02574ZZ, 02B74ZZ, 02570ZK, 02L70CK, 02L70DK, 02L70ZK, 02L73DK, 02L73CK, 02L73ZK, 02B70ZK, 02B73ZK, 02B74ZK
Postoperative outcomes	
Transfusion with red blood cells	ICD-9: 99.00, 99.01, 99.02, 99.03, 99.04
	ICD-10: 30233N1, 30243N1, 30253N1, 30233H0, 30243H0, 30253H0
Defibrillator Implantation	ICD-9: 37.96
	ICD-10: 0JH608Z, 0JH638Z, 0JH808Z, 0JH838Z
PPM	ICD-9: 37.80, 37.81, 37.82, 38.83
	ICD-10: 0JH604Z, 0JH604Z, 0JH634Z, 0JH804Z, 0JH834Z, 0JH605Z, 0JH635Z, 0JH805Z, 0JH835Z, 0JH606Z, 0JH636Z, 0JH806Z, 0JH836Z, 0JH60PZ, 0JH63PZ, 0JH80PZ, 0JH83PZ

BMI, Body mass index; *MI*, myocardial infarction; *CABG*, coronary artery bypass graft; *PCI*, percutaneous coronary intervention; *TAVR*, transcatheter aortic valve replacement; *LAAL*, left atrial appendage ligation; *PPM*, patient–prosthesis mismatch.

TABLE E2. Sensitivity analysis between adjusted models with and without Elixhauser score

Characteristic	Multivariable module				Sensitivity analysis			
	OR	95% CI	*P* value	VIF	OR	95% CI	*P* value	VIF
Elixhauser (*z* score)	2.10	1.87-2.36	<**.001**	1.4	-	-	-	-
Age (*z* score)	1.24	1.08-1.43	**.002**	2.0	1.33	1.16-1.52	<**.001**	2.1
Female sex	1.08	0.87-1.33	.5	1.3	1.02	0.83-1.25	.9	1.3
Race*								
Black	0.84	0.62-1.15	.3	1.1	0.81	0.60-1.10	.2	1.2
Hispanic	0.75	0.50-1.12	.2	1.1	0.77	0.52-1.14	.2	1.1
Year (*z* score)	0.93	0.82-1.06	.3	1.7	0.97	0.86-1.09	.6	1.7
Insurance†								
Medicare	0.98	0.70-1.35	.9	2.7	0.98	0.71-1.35	>.9	2.8
Private	0.69	0.49-0.97	**.033**	2.0	0.69	0.50-0.97	**.031**	2.0
Income 150% FPL	0.75	0.57-0.99	**.041**	1.1	0.76	0.58-0.99	**.043**	1.1
BMI >40	1.80	1.46-2.22	<**.001**	1.2	2.06	1.68-2.51	<**.001**	1.2
Dyslipidemia	0.76	0.62-0.94	**.011**	1.2	0.65	0.53-0.79	< **.001**	1.2
HTN	0.91	0.73-1.14	.4	1.3	0.76	0.62-0.93	**.009**	1.3
DM (no chronic complications)	1.32	1.05-1.66	**.017**	1.3	1.23	0.99-1.54	.062	1.3
DM (with chronic complications)	1.32	0.97-1.81	.081	1.5	1.54	1.13-2.11	**.006**	1.5
Previous MI	1.10	0.74-1.63	.6	1.5	1.06	0.72-1.57	.8	1.5
PAD	1.10	0.79-1.53	.6	1.1	1.34	0.97-1.85	.079	1.1
Afib	0.44	0.35-0.55	<**.001**	1.4	0.58	0.47-0.72	<**.001**	1.5
TIA	0.70	0.40-1.26	.2	1.1	0.68	0.39-1.20	.2	1.1
Ischemic stroke	2.75	0.92-8.24	.072	1.1	3.95	1.56-9.99	**.004**	1.1
Nonischemic stroke	0.95	0.68-1.33	.8	1.1	1.11	0.80-1.55	.5	1.1
COPD	0.75	0.59-0.95	**.016**	1.2	0.93	0.75-1.17	.6	1.2
End-Stage CKD	1.44	1.0-2.09	.053	1.3	2.14	1.50-3.04	<**.001**	1.3
CHF admission	1.39	0.85-2.27	.2	1.1	1.87	1.15-3.04	**.011**	1.1
CAD	1.01	0.79-1.30	>.9	1.7	1.05	0.82-1.35	.7	1.7
Redo after valve	1.63	1.01-2.63	**.044**	1.2	1.61	1.01-2.56	**.046**	1.2
Redo after CABG	1.36	0.88-2.09	.2	1.2	1.40	0.91-2.15	.12	1.2
Previous PCI	1.41	0.98-2.04	.067	1.3	1.27	0.90-1.81	.2	1.3
Endocarditis	1.24	0.89-1.72	.2	1.5	1.32	0.96-1.82	.083	1.5
Mitral regurgitation	0.99	0.79-1.23	.9	1.2	0.94	0.76-1.17	.6	1.2
Elective admission	0.70	0.56-0.87	**.001**	1.3	0.60	0.48-0.74	<**.001**	1.3
MV repair *(ref: replacement)*	0.58	0.46-0.73	<**.001**	1.2	0.49	0.38-0.61	<**.001**	1.2
Concomitant‡								
+CABG	1.66	1.22-2.25	**.001**	1.4	1.75	1.30-2.36	<**.001**	1.5
+AVR	1.82	1.37-2.40	<**.001**	1.4	1.89	1.43-2.49	<**.001**	1.4
+Ascending aorta	1.68	0.66-4.28	.3	1.1	2.39	0.94-6.09	.069	1.1
+TVR	1.20	0.84-1.72	.3	1.3	1.50	1.06-2.12	**.021**	1.3
>2 procedures	2.83	2.07-3.85	<**.001**	1.3	3.58	2.67-4.81	<**.001**	1.4
LAAL/maze	0.92	0.73-1.17	.5	1.3	0.91	0.72-1.15	.4	1.3

(Continued)

TABLE E2. Continued

Characteristic	Multivariable module				Sensitivity analysis			
	OR	95% CI	*P* value	VIF	OR	95% CI	*P* value	VIF
Model metrics	AUC/C-index: 82.64%				AUC/C-index: 77.98%			
	Brier score: 4.25%				Brier score: 4.40%			
	Min-Max VIF: 1.08-2.70				Min-Max VIF: 1.07-2.79			

Bold indicates $P < .05$. *OR*, Odds ratio; *VIF*, variance inflation factor; *FPL*, federal poverty level; *BMI*, body mass index; *HTN*, hypertension; *DM*, diabetes mellitus; *MI*, myocardial infarction; *PAD*, peripheral artery disease; *Afib*, atrial fibrillation; *TIA*, transient ischemic attack; *COPD*, chronic obstructive pulmonary disease; *CKD*, chronic kidney disease; *CHF*, congestive heart failure; *CAD*, coronary artery disease; *CABG*, coronary artery bypass graft; *PCI*, percutaneous coronary intervention; *MV*, mitral valve; *AVR*, aortic valve replacement; *TVR*, transcatheter aortic valve replacement; *LAAL*, left atrial appendage ligation; *AUC*, area under the curve. *Reference category: White/Other. †Reference category: uninsured/Medicaid. ‡Reference category: Isolated MV repair.

TABLE E3. Software packages and additional references

Package name	Package version	Use
survey[E1]	4.0	Calculations and statistics for complex survey designs
comorbidity[E2]	1.0.2	Computing Elixhauser comorbidity score
missRanger[E3]	2.1.3	Impute data with observation weights and fast random forest
randomForestSRC[E4-E6]	3.1.0	Fast Random Forests for unbalanced data with weighted observations
ggRandomForests[E7]	2.2.0	Create pretty plots from randomForestSRC objects
gtsummary[E8]	1.6.0	Creating pretty tables
flextable[E9]	0.7.2	Converting gtsummary tables into docx
officer[E10]	0.4.3	Modify docx file orientation and margins
fst[E11]	0.9.8	Load large NIS files fast
tidyverse[E12]	1.3.1	Collection of R packages designed for data science
cowplot[E13]	1.1.1	Combine 'ggplot2' plots
rms[E14]	6.3.0	"Regression Modeling Strategies" used for VIF
DescTools[E15]	0.99.45	Descriptive statistics for model performance
DataExplorer[E16]	0.8.2	Data exploration and assessment
skimr[E17]	2.1.5	Data exploration and assessment
tableone[E18]	0.13.2	Data exploration, assessment, and presentation
doParallel[E19]	1.0.17	To use multicore functionality and boost analysis speed
pacman[E20]	0.5.0	Conveniently call and install packages
R[E21]	4.2.2	R software package provides environment for statistical computing and graphics

NIS, Nationwide Inpatient Sample; *VIF*, variance inflation factor.

TABLE E4. In-hospital outcomes stratified by concomitant surgery

	Overall comparison			Concomitant surgery outcome details				
Characteristic	**Isolated MVR (n = 26,9601)**	**Concomitant MVR (n = 21,8151)**	***P* value***	**+CABG (n = 68,251)**	**+AVR (n = 65,401)**	**+AscendingAo (n = 2651)**	**+TVR (n = 48,551)**	**>2 procedures (n = 33,301)**
In-hospital mortality	850 (3.2)	1580 (7.2)	**<.001**	435 (6.4)	470 (7.2)	25 (9.4)	230 (4.7)	420 (13)
Unknown	10	10		5	5	0	0	0
Wound complications	210 (0.8)	250 (1.1)	.067	60 (0.9)	80 (1.2)	15 (5.7)	45 (0.9)	50 (1.5)
Valve complications	445 (1.7)	600 (2.8)	**<.001**	110 (1.6)	210 (3.2)	cell size ≤10†	140 (2.9)	130 (3.9)
Bleeding complications	14,080 (52)	12,500 (57)	**<.001**	3675 (54)	3910 (60)	150 (57)	2740 (56)	2025 (61)
Transfusion	5540 (21)	5995 (27)	**<.001**	1945 (28)	1945 (30)	60 (23)	1105 (23)	940 (28)
Complete heart block	3495 (13)	3735 (17)	**<.001**	735 (11)	1290 (20)	25 (9.4)	1000 (21)	685 (21)
Cardiac arrest	1245 (4.6)	1385 (6.3)	**<.001**	365 (5.3)	425 (6.5)	cell size ≤10†	320 (6.6)	265 (8.0)
Permanent stroke	140 (0.5)	115 (0.5)	>.9	35 (0.5)	45 (0.7)	0 (0)	cell size ≤10†	30 (0.9)
Perioperative MI	950 (3.5)	2595 (12)	**<.001**	1860 (27)	255 (3.9)	cell size ≤10†	75 (1.5)	400 (12)
Acute renal failure	6570 (24)	8340 (38)	**<.001**	2545 (37)	2520 (39)	100 (38)	1660 (34)	1515 (45)
CIED	115 (0.4)	105 (0.5)	.7	25 (0.4)	30 (0.5)	cell size ≤10†	30 (0.6)	15 (0.5)
Permanent Pacemaker	5555 (21)	6055 (28)	**<.001**	1945 (28)	1980 (30)	60 (23)	1115 (23)	955 (29)

Values are presented as n (%). Bold indicates $P < .05$. *MVR*, Mitral valve replacement; *CABG*, coronary artery bypass grafting; *AVR*, aortic valve replacement; *AscendingAo*, aortic surgery; *TVR*, tricuspid valve replacement; *MI*, myocardial infarction; *CIED*, Implantable cardioverter defibrillator. *$\chi 2$ test with Rao and Scott's second-order correction comparing isolated to concomitant MVR, without consideration for multiple subgroups of concomitant MVR. †Healthcare Cost and Utilization Project privacy protection policy does not allow sharing this information.