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Utilization of mechanical prostheses and outcomes of surgical aortic valve replacement at safety net hospitals



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ABSTRACT

Background: Safety-net hospitals care for a high proportion of uninsured/underinsured patients who may lack access to longitudinal care. The present study characterized the use of mechanical valves and clinical outcomes of surgical aortic valve replacement at safety net hospitals.

Methods: All adults undergoing surgical aortic valve replacement were abstracted from the 2016–2018 Nationwide Readmissions Database. Hospitals were divided into quartiles based on volume of all Medicaid and uninsured admissions, with the highest quartile defined as safety net hospitals. Multivariable regression was used to determine the association between safety net hospitals and several outcomes including mechanical valve use, perioperative complications, index hospitalization costs, 90-day readmission, and complications at readmission.

Results: Of the 94,580 patients undergoing surgical aortic valve replacement, 14.5% of operations were at safety net hospitals. Patients at safety net hospitals more commonly received mechanical valves (20.3% vs 16.9%, P < .01) compared to those at non–safety net hospitals. After adjustment, safety net hospitals remained associated with a greater odds of mechanical aortic valve use (adjusted odds ratio, 1.13, 95% confidence interval 1.05–1.21). However, operation at safety net hospitals was also associated with increased odds of perioperative complications (adjusted odds ratio 1.10, 95% confidence interval 1.03–1.17) and higher hospitalization costs (β coefficient +\$6.15K, 95% confidence interval +\$5.26 - +\$7.03) despite similar 90-day readmissions. Upon readmission, safety net hospitals patients were more likely to experience mortality (adjusted odds ratio 1.87, 95% confidence interval 1.18–2.98) and stroke (adjusted odds ratio 2.41, 95% confidence interval 1.23–4.70) compared to those at non–safety net hospitals.

Conclusion: Hospital safety net status is associated with increased use of mechanical valves for surgical aortic valve replacement despite also being associated with increased perioperative complications, costs, and significant complications upon readmission. Ability to access adequate follow-up care may be an important consideration for surgical aortic valve replacement at safety net hospitals.

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INTRODUCTION

Commonly used prostheses for surgical aortic valve replacement (SAVR) may be either biologic (bovine or porcine tissue) or mechanical, with both materials carrying their drawbacks and merits [1]. While

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bioprosthetic valves obviate the need for long-term anticoagulation, they suffer from structural deterioration and necessitate reoperation within approximately 10–15 years [2–5]. Mechanical valve replacement is a more durable alternative with a potential long-term mortality benefit over bioprosthetic SAVR. However, mechanical valves are thrombogenic and require lifelong anticoagulation to prevent thromboembolic complications [4,5]. Given these considerations, a shared decision-making approach accounting for patient lifestyle and priorities is a pivotal component of the workup for SAVR.

This decision may be even more challenging in the setting of safety net hospitals (SNH) which care for a high proportion of uninsured or underinsured patients. Such hospitals aim to treat patients regardless of their ability to pay [6] and have been linked to inferior outcomes compared to others across a multitude of operations [7,8]. This observation may be attributable to a relative lack of resources, with patients at SNH often facing significant barriers to adequate longitudinal care

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Abbreviations: β , β coefficient; 95% CI, 95% confidence interval; AOR, adjusted odds ratio; *ICD-10, International Classification of Disease 10th Revision*; NRD, Nationwide Readmissions Database; SAVR, surgical aortic valve replacement; SNH, safety net hospital; US, United States.

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[9–11]. Such constraints may be particularly impactful in patients undergoing SAVR with mechanical prosthesis, which necessitates routine follow-up and adherence to a daily anticoagulation regimen.

Whereas the clinical outcomes of mechanical vs bioprosthetic SAVR have been extensively studied in the general population, data regarding their performance in the setting of safety net hospitals are lacking. Thus, the present study characterized the association of SNH with use of mechanical valves in SAVR in a contemporary national sample while also evaluating clinical and financial outcomes of SAVR at SNH. We hypothesized that SNH would be associated with higher utilization of mechanical valves and worse perioperative outcomes compared to non-SNH.

METHODS

All adult (age \geq 18 years) hospitalizations for isolated, elective SAVR were tabulated from the 2016–2018 Nationwide Readmissions Database (NRD). Maintained as part of the Healthcare Cost and Utilization Project, the NRD is the largest all-payer readmission database in the United States (US) and captures administrative data from 28 participating states. Each inpatient hospitalization in the NRD is linked to a unique identifier, allowing for subsequent readmissions to be tracked within a given calendar year. Using validated survey-weighted methodology, the NRD provides accurate national estimates from 59% of hospitalizations in the US.

Operations, diagnoses, and comorbidities were ascertained using International Classification of Disease 10th Revision (ICD-10) codes [12], whereas demographics and hospital characteristics were derived from available NRD fields [13]. Patients with a history of endocarditis or missing key data including age, sex, and mortality were excluded from analysis (7.0%). All subjects were further stratified according to the type of prosthesis received (mechanical versus bioprosthetic). Hospitals were grouped into quartiles based on the proportion of all admissions classified as underinsured (Medicaid or self-pay), with the highest quartile considered safety net hospitals (SNHs) and the remainder as non-SNH [14]. Definitions of self-pay were determined using the HCUP data elements and encompass those who are uninsured and ineligible for government assistance [13]. The van Walraven modification of the Elixhauser comorbidity index was used to evaluate the overall burden of chronic conditions, as previously described [15]. Hospitalization charges were converted to costs using center-specific cost-to-charge files and adjusted for inflation to the 2018 Personal Health Care Expenditure [16].

The primary study end point was utilization of mechanical prostheses for SAVR. Several secondary outcomes were evaluated and included inhospital mortality, complications, length of stay, hospitalization costs, unplanned readmissions within 90 days of index discharge, and primary reason for rehospitalization. Complications included stroke, deep vein thrombosis (DVT)/pulmonary embolism (PE), cardiac complications (cardiac arrest, ventricular tachycardia, ventricular fibrillation, and cardiac tamponade), sepsis, and surgical site infections (*ICD-10* codes previously described) [12]. All complications were evaluated at both index hospitalization and 90-day readmissions.

Patient and hospital-level factors were compared using the adjusted Wald and χ^2 tests where appropriate. Freedom from readmission was visualized using Kaplan–Meier survival analysis, and significance was determined using the log-rank test.

Entropy balancing for causal effects was used to adjust for differences in characteristics between study cohorts for all other models [17]. This method is based on pseudopropensity scores and finds the set of sample weights that allows for the optimal covariate balance between cohorts [17,18]. Entropy balancing allows for the retention of all observations and provides more robust covariate balance compared to traditional pairwise methods [19,20]. Multivariable logistic and linear regression models were constructed to determine independent associations between SNH and study outcomes. Covariates for all models were selected using the elastic net regularization method, which uses a penalized least squares methodology to account for collinearity and select variables, as previously described [21]. Briefly, this method uses 10fold cross-validation to evaluate different models and select the set of covariates that maximizes the area under the receiver operating characteristic curve (*C*-statistic). Final covariates included in multivariable analysis can be seen in Supplementary Table 1. Hospitals were divided into low-, mid-, and high-volume centers based on tertiles of annual valvular operative volume for multivariable analyses. All adjusted outcomes are reported as adjusted odds ratios (AORs) or β coefficients (β) with 95% confidence intervals (95% CIs) for categorical and continuous outcomes, respectively. This study was deemed exempt from full review by the University of California, Los Angeles, Institutional Review Board. All statistical analyses were performed using Stata 16 (StataCorp, College Station, TX).

RESULTS

Characteristics of Patients Undergoing SAVR. Of an estimated 94,580 patients undergoing SAVR, 14.5% of operations were at SNH (Table 1). Patients at SNH were, on average, younger (64.1 vs 65.6 years, P < .001), more frequently in the bottom quartile of income (24.9% vs 20.2%, P < .01), and more commonly on Medicaid or self-pay (13.9% vs 6.7%, P < .001). Further breakdown of demographics by safety net quartile are displayed in Supplementary Table 2. Despite an overall similar Elixhauser comorbidity index (4.7 vs 4.7, P = .25), patients at SNH had higher rates of diabetes (28.0% vs 25.3%, P < .01), congestive heart failure (35.6% vs 32.6%, P = .04), and end-stage renal disease (2.1% vs 1.7%, P = .03) compared to those at non-SNH (Table 2).

Hospitals classified as SNH were less likely to be high volume (73.8% vs 82.9%, P < .001) and more commonly categorized as urban teaching hospitals (90.6% vs 82.9%, P < .001) compared to their non-SNH counterparts. Mechanical valve prostheses were used in 17.4% of cases overall and were more frequently utilized at SNH compared to non-SNH (20.3% vs 16.9%, P < .01).

Factors Associated With Mechanical Valve Utilization. Patient and hospital-level factors associated with mechanical valve use are reported in Table 3 (model *C*-statistic = 0.75). After adjustment, hospital safety

Table 1

Baseline characteristics of patients undergoing SAVR

Variable	SNH	Non-SNH	P value
	n = 13,722 (14.5%)	n = 80,857 (85.5%)	
Mechanical prosthesis	20.3	16.9	<.01
Age	64.1 ± 0.2	65.6 ± 0.1	<.001
Female	36.9	36.0	.23
Income quartile			.02
76th-100th	21.4	23.5	
51st-75th	25.8	28.5	
26th-50th	28.0	27.9	
0–25th	24.9	20.2	
Payer			<.001
Private	32.6	35.5	
Medicare	53.4	57.8	
Medicaid	9.7	4.0	
Self-pay	1.2	0.9	
Other*	3.0	1.8	
Elixhauser comorbidity index	4.74 ± 0.04	4.69 ± 0.02	.25
Hospital volume tertile			<.001
Low volume	3.2	1.3	
Mid volume	23.0	15.8	
High volume	73.8	82.9	
Hospital teaching status			<.001
Rural	1.0	2.0	
Urban nonteaching	8.5	15.2	
Urban teaching	90.6	82.9	

Values are expressed % of population or mean \pm standard error.

* Other payer defined as "no charge" or "other" by the Healthcare Cost and Utilization Project.

Table 2

Comorbidities of patients undergoing SAVR

Variable	SNH	Non-SNH	P value
Congestive heart failure	35.6	32.6	.04
Coronary artery disease	33.2	34.7	.10
Arrhythmia	55.4	55.9	.54
Chronic atrial fibrillation	27.4	28.9	.05
Hypertension	26.7	25.9	.56
Chronic obstructive pulmonary disease	19.4	18.8	.36
Pulmonary circulatory disorder	9.4	9.3	.84
Peripheral vascular disease	27.9	28.6	.44
Diabetes	28.0	25.3	<.01
Psychiatric disorders	10.1	9.9	.63
Malignancy	1.5	1.4	.49
Neurologic complications	5.3	5.3	.87
Hypothyroidism	12.9	12.8	.85
Anemia	3.2	2.7	.12
Chronic kidney disease	1.7	1.4	.06
End-stage renal disease	2.1	1.7	.03
Liver disease	3.3	3.0	.20

Values are expressed % of population or mean \pm standard error.

net status remained associated with increased odds of receiving a mechanical valve (AOR 1.13, 95% CI 1.05–1.21) compared to operation at non-SNH. Other factors associated with mechanical valve use included female sex (AOR 1.08, 95% CI 1.00–1.18) and several preexisting conditions including congestive heart failure (AOR 1.16 95% CI 1.05–1.27), peripheral vascular disease (AOR 1.16, 95% CI 1.09–1.28), and diabetes (AOR 1.16, 95% CI 1.06–1.28).

Conversely, increasing age (AOR 0.93/y, 95% CI 0.93–0.93), increasing year of operation (AOR 0.91/y, 95% CI 0.87–0.95), coronary artery disease (AOR 0.91, 95% CI 0.84–0.99), malignancy (AOR 0.68, 95% CI 0.49–0.93), and anemia (AOR 0.79, 95% CI 0.64–0.98) were all associated with decreased odds of mechanical valve use.

Index Outcomes of SAVR at SNH. Unadjusted outcomes of SAVR at index hospitalization are shown in Table 4. Patients at SNH experienced similar rates of in-hospital mortality (1.9% vs 1.6%, P = .19) despite higher rates of perioperative complications (28.4% vs 25.8%, P < .01) including cardiac (7.3% vs 5.9%, P < .001), sepsis (1.5% vs 1.1%, P < .01), and surgical site infections (0.7% vs 0.5%, P < .01) (Supplementary Table 3). Additionally, patients at SNH experienced longer lengths of stay (9.0 vs 8.5 days, P

Table 3

Factors associated with mechanical valve use in SAVR

Recipient variable	Odds ratio	95% CI	P value
Safety net hospital	1.13	1.05-1.21	<.01
Female	1.08	1.00-1.18	.05
Age, per 1 y	0.93	0.93-0.93	<.001
Year of operation, 2016–2018	0.91	0.87-0.95	<.001
Hospital volume tertile			
Small	Reference	Reference	Reference
Medium	0.94	0.74-1.20	.63
Large	0.79	0.62-1.02	.07
Hospital teaching status			
Rural	Reference	Reference	Reference
Urban nonteaching	1.00	0.70-1.43	1.00
Urban teaching	0.83	0.59-1.18	.30
Elixhauser comorbidity index, per 1 U	0.96	0.93-1.00	.05
Congestive heart failure	1.16	1.05-1.27	<.01
Coronary artery disease	0.91	0.84-0.99	.02
Pulmonary circulatory disorder	1.16	1.06-1.27	<.01
Peripheral vascular disease	1.16	1.09-1.23	<.001
Diabetes	1.16	1.06-1.28	<.01
Malignancy	0.68	0.49-0.93	.02
Anemia	0.79	0.64-0.98	.03

C-statistic = 0.75.

Covariates not shown above include arrhythmia, chronic atrial fibrillation, hypertension, chronic obstructive lung disease, psychiatric disorders, neurologic complications, hypo-thyroidism, chronic kidney disease, end-stage renal disease, and liver disease.

< .001) and higher costs (\$54.7K vs \$47.1K, P < .001) but lower rates of non-home discharge (20.0% vs 25.6%, P < .001) compared to non-SNH.

Following adjustment, operation at SNH remained associated with higher odds of perioperative complications (AOR 1.10, 95% CI 1.03–1.17) including cardiac (AOR 1.18 95% CI 1.05–1.32), sepsis (AOR 1.34 95% CI 1.05–1.71), and surgical site infections (AOR 1.42 95% CI 1.02–2.00) compared to non-SNH (Fig 1). Additionally, those at SNH were associated with longer lengths of stay (β + 0.24 days, 95% CI 0.09–0.40 days) and higher hospitalization costs (β + \$6.15K, 95% CI + \$5.26–+\$7.03) (Table 4). However, hospital safety net status remained associated with lower odds of non-home discharge (AOR 0.71, 95% CI 0.64–0.78) with non-SNH as reference.

Outcomes of SAVR at Readmission. Kaplan–Meier estimates revealed patients at SNH to have similar freedom from readmission at 90 days following discharge (85.7% vs 86.0%, log-rank P = .67, Fig 2). Following adjustment, operation at SNH was associated with similar odds of 90-day readmissions compared to non-SNH (AOR 1.00, 95% CI 0.91–1.10) (Table 4).

Among patients readmitted within 90 days of discharge, those receiving their initial operation at SNH exhibited higher rates of mortality (4.7% vs 2.6%, P < .01) and stroke (2.0% vs 1.1%, P = .44) despite similar rates of DVT/PE (3.5% vs 3.4%, P = .88), cardiac complications (9.9% vs 9.0%, P = .44), sepsis (13.6% vs 12.5%, P = .40), and surgical site infections (6.4% vs 5.7%, P = .49) compared to non-SNH patients (Supplementary Table 4). Following adjustment, index hospitalization at SNH remained associated with increased odds of mortality (AOR 1.87, 95% CI 1.18–2.98) and stroke (AOR 2.41, 95% CI 1.23–4.70) among those readmitted (Fig 3).

Complications upon readmission by valve type can be seen in Supplementary Table 5. Among bioprosthetic valve recipients, SNH was associated with increased odds of mortality (AOR 1.66, 95% CI 1.01–2.73) but similar odds of DVT/PE (AOR 1.01, 95% CI 0.62–1.65) and stroke (AOR 1.62, 95% CI 0.73–3.61) upon 90-day readmission. However, among those receiving mechanical prostheses, SNH was associated with increased odds of mortality (AOR 3.54, 95% CI 1.24–10.11), DVT/PE (AOR 9.72, 95% CI 1.24–76.36), and stroke (AOR 14.49, 95% CI 3.03–69.35) upon readmission within 90 days of discharge.

Discussion

The decision between mechanical and biologic prostheses for SAVR remains multifactorial, with extensive consideration given toward patient preferences and lifestyle. Although several studies have evaluated the clinical outcomes of mechanical and bioprosthetic SAVR in the general population [5,22–24], there is a paucity of such literature in the setting of highly burdened safety net centers. In the present study, we found SNH to be associated with increased use of mechanical prostheses for isolated, elective SAVR. Additionally, we found SAVR at SNH to be associated with higher odds of perioperative complications, longer lengths of stay, and higher hospitalization costs despite similar odds of readmissions at 90 days following discharge. Upon readmission, however, patients undergoing initial operation at SNH exhibited higher adjusted rates of mortality and stroke compared to those at non-SNH.

Patients in the setting of SNH often face complex socioeconomic challenges and barriers to care that warrant special consideration of such factors prior to operation. These include the ability to adhere to strict anticoagulation regimens necessitated by mechanical valves [25]. Although prior studies have identified several patient-level factors associated with mechanical valve use in the general population [26], none have examined this association in the context of SNH. Recent reports by Alkhouli et al found female sex and the presence of peripheral vascular disease to be associated with mechanical valve use, whereas increasing age and hospital teaching status were negatively associated with mechanical valve use [26]. Our findings were largely in accordance

Table 4

Index outcomes of SAVR at SNH

	Unadjusted			Adjusted	
Complication	SNH	Non-SNH	P value	Odds ratio/β coefficient (95% CI)	P value
Mortality	1.9	1.6	.19	1.02 (0.82–1.27)	.84
Perioperative complication	28.4	25.8	<.01	1.10 (1.03–1.17)	<.01
Length of stay (d)	7.6 ± 0.1	7.1 ± 0.1	<.001	+0.24(0.09 - +0.40)	<.01
Hospitalization cost (\$,1000 USD)	54.7 ± 1.1	47.1 ± 0.6	<.001	+6.15(+5.26-+7.03)	<.001
Non-home discharge	20.0	25.6	<.001	0.71 (0.64-0.78)	<.001
90-d nonelective readmission	10.5	10.2	.51	1.00 (0.91–1.10)	.99

Non-SNH reference for each value; unadjusted values shown as rates (%) or mean (\pm SE).

with this prior literature, building upon such findings by accounting for hospital-level safety net burden.

In our study, we found SNH to be associated with an increase in relative odds of mechanical valve use compared to non-SNH. This finding may reflect the increased operative difficulty of certain biologic valve procedures such as stentless xenograft implantation [27] and the Ross procedure [28,29]. Such procedures necessitate a large, experienced surgical team that some safety net centers may lack [30]. Moreover, SNH may also not have access to newer generations of bioprosthetic valves that have been associated with improved durability [31], leading to the increased use of mechanical prostheses in the absence of other long-term alternatives.

In addition to increased rates of mechanical valve use, we found SNH to be associated with a significant detriment in clinical outcomes compared to non-SNH at both index hospitalization and upon readmission. Patients at SNH experienced a 10% increase in adjusted odds of perioperative cardiac complications, along with significantly longer lengths of stay and higher hospitalization costs. Such findings may be indicative of a relative lack of resources at SNH that translate to poorer operative outcomes for patients in this setting. Additionally, SAVR patients at SNH experienced higher rates of sepsis and surgical site infections. This may suggest that the consequences of resource scarcity may extend beyond the immediate operative period to include relatively worse wound care and management in the days ensuing operation.

This notion may be further supported by the persistence of worse outcomes at SNH among those readmitted within 90 days of discharge. We observed patients undergoing initial operation at SNH to have higher mortality and stroke upon readmission compared to those at



Fig 1. Association of hospital safety net status with complications following surgical aortic valve replacement. Adjusted odds ratios shown for operations occurring at safety net hospitals, with non–safety net hospitals as reference. Cardiac complications include cardiac arrest, ventricular tachycardia, ventricular fibrillation, and tamponade.

non-SNH. These differences were significantly magnified among those receiving mechanical valves, with SNH being associated with 3.5-, 9-, and 14-fold increases in odds of mortality, DVT/PE, and stroke upon re-admission, respectively. Given that the detriment of SNH was potentiated among mechanical valve recipients, the higher rates of stroke may reflect relatively poor monitoring of anticoagulation response and adherence to medication in this cohort. Mechanical valves require early heparin bridging with several international normalized ratio (INR) measurements in the weeks following operation. Patients at SNH may lack the ability to adhere to such rigid postoperative regimens due to extrinsic factors including hospital distance, access to transportation, and price of medication, among several other socioeconomic barriers to care.

These findings build upon prior literature examining the impact of hospital safety net burden on outcomes following SAVR [32]. Early reports by Ando and colleagues found hospital safety net burden to be associated with longer lengths of stay despite no differences in mortality. Previous reports, however, failed to account for several key cardiovascular complications that we found to be increased at SNH in our study. Such complications, including cardiac arrest, ventricular tachycardia, ventricular fibrillation, and cardiac tamponade, may be more sensitive markers of operative performance than in-hospital mortality in the setting of generally low-risk procedures such as elective SAVR. Furthermore, we found the detriment of hospital safety net burden to manifest primarily at readmission, including increased odds of mortality and stroke. This may indicate that the detriment associated with SNH may be partially attributed to factors beyond index hospitalization such as poor follow-up, socioeconomic barriers to care, and insufficient attainment of INR goals. Taken together, our findings may suggest that physicians at SNH should (a) routinely evaluate socioeconomic barriers to follow-up care as part of the workup for SAVR, (b) take extra caution to ensure adequate postoperative management including wound care



Fig 2. Kaplan–Meier freedom from readmission following surgical aortic valve replacement at SNH versus non-SNH.



Fig 3. Association of hospital safety net status with complications upon 90-day readmission following surgical aortic valve replacement. Adjusted odds ratios shown for operations occurring at safety net hospitals, with non-safety net hospitals as reference. Cardiac complications include cardiac arrest, ventricular tachycardia, ventricular fibrillation, and tamponade.

and meeting of INR goals, and (c) encourage development of multidisciplinary heart teams capable of more complex valvular procedures, which may circumvent the need mechanical prostheses.

This study has several important limitations. The NRD is an administrative, large-scale database that lacks clinical granularity, including features such as specific brands of prostheses used, use and adherence to anticoagulant therapy, and the presence of patient-prosthesis mismatch in SAVR. Similarly, specific indications for SAVR (stenosis versus regurgitation) and more granular data including valve area, transvalvular pressure gradient, left ventricular function, or New York Heart Association class were not available in the database. Thus, it is possible that mechanical valves were used more often at SNH due to a different set of surgical indications in this patient population. However, all available covariates including several specific patient comorbidities were considered in multivariable analysis and selected using previously validated methods [15,17,21]. We were not able to discern the severity or timing of specific complications beyond the admission during which they occurred due to limitations of the database. Finally, the NRD does not track long-term survival or events that occur outside of hospitalization. Thus, we were not able to report differences in long-term mortality between treatment groups.

Given these constraints, further investigation into the long-term outcomes of SAVR at SNH is warranted. Specifically, future studies should aim to evaluate long-term survival differences among patients undergoing SAVR at SNH versus non-SNH. Furthermore, investigation into the optimal prosthesis type for SAVR in the setting of SNH is warranted. Future investigation may be performed using the Society of Thoracic Surgeons data, which have been previously linked to the Centers for Medicare and Medicaid Services and have been helpful for determining outcomes in the elderly. However, the most definitive method would be a multi-institutional, randomized clinical trial with participation of both safety net and non–safety net hospitals, but it would take years to complete. Future work may use state inpatient databases that can be linked to Centers for Medicare and Medicaid Services data and provide long-term outcomes.

In the present study, we found hospital safety net status to be associated with increased use of mechanical valves for isolated SAVR. Additionally, we found operation at SNH to be associated with increased perioperative complications, longer lengths of stay, and higher hospitalization costs. Upon readmission, patients undergoing initial operation at SNH had higher rates of mortality and stroke compared to those at non-SNH. Further work will be necessary to determine whether social factors such as access to anticoagulation therapy and barriers to follow-up care are driving the findings of this study.

Author Contribution

Samuel T. Kim: Conceptualization, Methodology, Formal analysis, Writing, Zachary Tran: Methodology, Validation, Writing. Yu Xia: Validation, Writing, Supervision. Vishal Dobaria: Formal analysis, Methodology, Validation. Ayesha Ng: Formal analysis, Methodology, Writing. Peyman Benharash: Conceptualization, Methodology, Validation, Writing, Supervision.

Conflict of Interest

The authors declare no conflicts of interest.

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Ethic Approval

This study was deemed exempt from full review by the University of California, Los Angeles, Institutional Review Board.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.sopen.2022.04.001.

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