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Article

Surgical Ablation for Atrial Fibrillation in Mitral Valve Surgery: Improved Survival and Stroke Risk in US Veterans

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Abstract

Background: Surgical ablation for atrial fibrillation (AF) is strongly recommended in patients undergoing mitral valve (MV) surgery but is underutilized. Left atrial appendage occlusion (LAAO) in patients with AF undergoing cardiac surgery is a matter of debate, and it is not clear which patients derive long-term benefit. This issue has not been investigated in United States Veterans. **Methods**: We performed a retrospective review of 1289 patients with preoperative AF who underwent MV surgery between 2010–2020. Patients were grouped based on whether their procedure included ablation and LAAO, LAAO without ablation, or neither. Cox proportional hazard models, adjusted for covariates, were used to calculate risk for stroke, myocardial infarction (MI), and death based on intervention. **Results**: Ablation was performed in 645/1289 (50.0%) of patients and LAAO without ablation was performed in 186/1289 (14.4%) patients. Mean follow-up was 4.1 ± 3.1 years. Patients who underwent ablation had a 62% lower long-term risk of stroke (0.38, 95% CI: 0.22–0.67, $p < 0.001$) and 20% lower long-term mortality risk (adjusted hazard ratios (aHR) 0.80, 95% CI: 0.66–0.95, $p = 0.012$), but no difference in risk of MI (aHR 0.67, 95% CI: 0.38–1.16, $p = 0.15$). LAAO was not associated with differences in long-term risk of stroke, MI, or death. There were no differences in perioperative complications between groups. **Conclusions**: In veterans with AF undergoing MV surgery, ablation was inversely and independently associated with long-term stroke risk and long-term mortality, with no increased risk of perioperative complications. LAAO did not reduce long-term stroke risk.

Keywords

atrial fibrillation; ablation; mitral valve; MAZE; left atrial appendage occlusion

Introduction

Atrial fibrillation (AF) is a prevalent disease, with more than 37.5 million cases worldwide as of 2017, and an estimated increase global prevalence of over 60% by 2050 [1]. Preoperative AF is common in patients undergoing mitral valve (MV) surgery, with a reported incidence of 29% [2]. Significant efforts have been made to develop surgical treatments to reduce long-term morbidity associated with AF, especially stroke [3,4]. Surgical ablation for AF can be performed at the time of other procedures without increased risk of mortality or major morbidity, and is recommended during MV operations to restore sinus rhythm [5–7]. Between 2005–2010, 61.5% of patients with preoperative AF undergoing MV replacement (MVR) underwent concomitant ablation [2].

It has been hypothesized that cardioembolic strokes in patients with AF are due to thrombus generated in the left atrial appendage, and this has inspired the development of procedures to occlude, resect, or obliterate the appendage to decrease long-term stroke risk [8]. The LAAOS III trial demonstrated decreased risk of stroke or embolism in patients with AF after undergoing cardiac surgery with concomitant left atrial appendage occlusion (LAAO) when compared with patients who did not undergo LAAO [9]. The procedure has thus gained significant traction, with the development of specialized devices [10] and an increased number of procedures being performed [11].

This study aimed to evaluate utilization and long-term outcomes of surgical ablation for AF and LAAO without ablation in United States (US) veterans with AF undergoing MV repair or replacement within the Veterans Health Administration (VHA). The VHA delivers care to over 9.6 million veterans and includes 43 medical centers that perform cardiac surgery [12]. Veterans have overall poorer health and more medical comorbidities than the civilian population and have unique medical needs due to combat exposure and increased prevalence of stress and trauma related disorders [13–16].

Materials and Methods

Study Population

Records were obtained via the Veterans Affairs (VA) Surgical Quality Improvement Program (VASQIP) and the Corporate Data Warehouse (CDW) via the VA Informatics and Computing Infrastructure (VINCI). These databases prospectively collect preoperative, intraoperative, postoperative, and outcomes data on patients who undergo cardiac surgery at any of 43 VA cardiac surgery centers in the United States [17,18]. External studies have demonstrated consistent reliability of the data [17,19].

Institutional review board approval and a waiver of informed consent was obtained from the Washington, D.C. VA Medical Center. Patient selection and cohort determination is depicted in Fig. 1. Data were retrospectively reviewed from 1289 identified patients who underwent MV surgery between 1 January 2010 and 31 December 2020, and had a preoperative diagnosis of AF. Patients were identified using standard Common Procedure Terminology (CPT) codes (33425, 33426, 33427, 33430), and filtered to exclude patients with no previous diagnosis of AF. Patients were excluded if they had active endocarditis or if no operative data or report was available. Patients were then divided into three cohorts based on the type of surgical intervention they underwent at the time of their MV operation: surgical ablation plus LAAO, LAAO without ablation, or no ablation or LAAO. Patients undergoing ablation for AF were not further subdivided based on the lesion set performed, for example left atrial versus bi-atrial, or the ablative technology used (e.g., radiofrequency versus cryoablation).

Patient demographics, preoperative data, operative variables, perioperative outcomes, and long-term outcomes were compared among groups. Date of death was determined via VINCI, which is linked with Veterans Health Administration vital status files, Social Security Administration, Center for Medicare and Medicaid Services, and the National Cemetery Administration. Follow-up was completed through 31 December 2020. Mean follow-up of the entire cohort was 4.1 $\pm$ 3.1 years. The primary outcome of this study was all-cause mortality. Secondary outcomes included incidence of stroke (including transient ischemic attack (TIA)), MI, and perioperative complications.

Statistical Analysis

Preoperative demographics, patient characteristics, clinical comorbidities, 30-day outcomes, 1-year outcomes, and long-term outcomes were compared between cohorts at the univariable level. Continuous variables were compared with independent *t*-test or Mann Whitney U tests. Categorical variables were compared using Chi square tests. Comparisons of demographics, patient characteristics, and clinical comorbidities resulting in a *p*-value < 0.20 were considered potential confounding covariates and were adjusted for in multivariable analysis to better elucidate the independent effect of operative intervention on outcomes of interest. A time-to-event analysis was then used to test the primary hypothesis among the three groups with the use of Kaplan–Meier survival curves and log-rank testing. The treatment effects on risk for all-cause mortality, stroke/TIA, and MI were estimated as a hazard ratio with a 95% confidence interval, which was derived using a Cox proportional-hazards model. All multivariable models implemented a backward stepwise selection procedure of covariates triangulated with a purposeful selection approach using stay criteria of $\alpha = 0.1$. Confounding covariates for adjustment included: weight (kg), age, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, cardiomegaly, cerebrovascular disease (CVD), Class III or IV heart failure, renal failure, chronic obstructive pulmonary disease (COPD), moderate to severe coronary artery disease (CAD), CHA2DS2-VASc Score, smoking status, diabetes mellitus, functional status (FST), hypertension, peripheral vascular disease (PVD), prior heart surgery history, prior MI, sex, race, and pre-operative intra-aortic balloon pump (IABP). Adjusted hazard ratios (aHR) are reported for long-term outcomes along with 95% CI. *p*-values < 0.05 using two sided tests were considered statistically significant. All statistical analyses were performed using SPSS software version 29 (IBM SPSS Statistics for Windows, Version 29, IBM Corp, Armonk, NY, USA).

Results

Demographics

A total of 1289 patients met inclusion criteria: 645 patients (50.0%) underwent ablation and LAAO, 186 patients (14.4%) underwent LAAO without ablation, and 458 patients (35.5%) underwent neither ablation nor LAAO. We did not identify any patients in this cohort who underwent ablation without left atrial appendage occlusion.

Patients who did not undergo ablation or LAAO were slightly older and had higher incidence of several comorbidities including moderate or severe CAD, class IV heart failure, PVD, COPD, and history of cerebrovascular disease when compared with patients undergoing LAAO or surgical ablation (Table 1). These patients more commonly had prior heart surgery. Ablation patients had lower CHADS-VASC scores when compared with the other two groups.

Operative Characteristics and Outcomes

Mean follow-up for the entire cohort was 4.1 $\pm$ 3.1 years. Patients in the ablation group underwent fewer MV replacements than patients in the LAAO or No Abla-

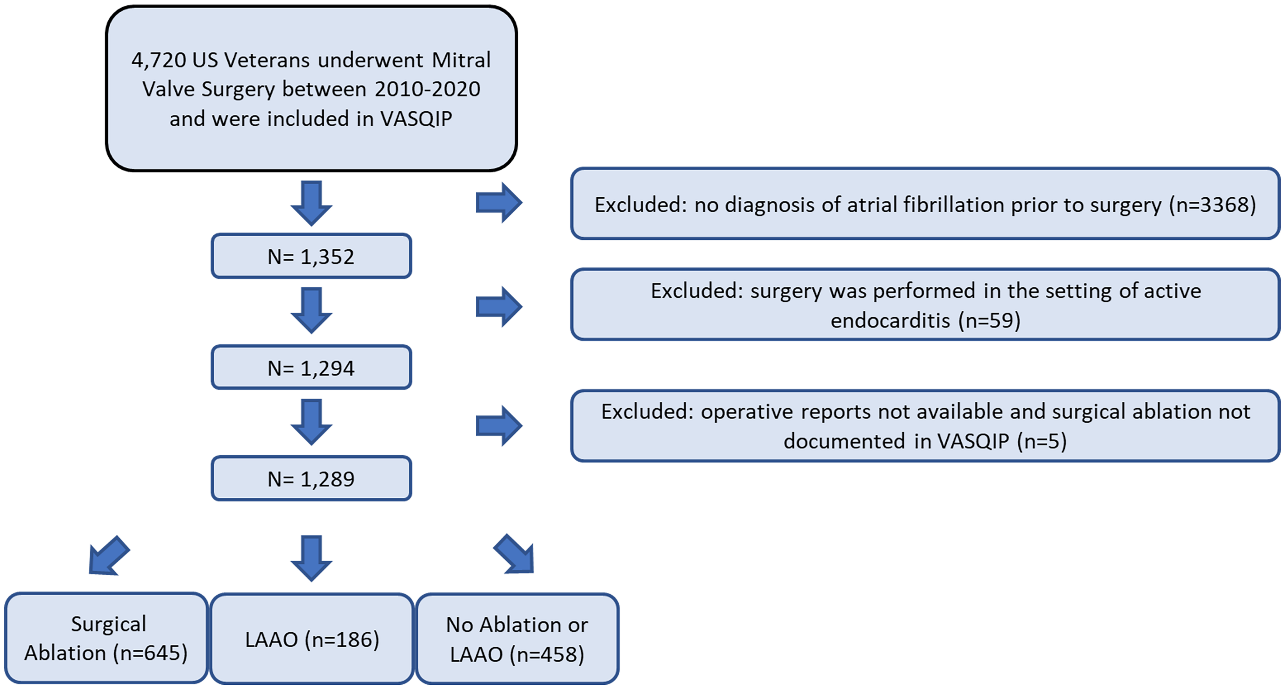

Fig. 1. Population selection and group assignments. Total number of included subjects was 1289. LAAO, Left Atrial Appendage Occlusion; VASQIP, Veterans Affairs Quality Improvement Program.

tion/LAAO groups (38.5% *vs.* 59% *vs.* 55.4%, $p < 0.001$) and fewer concomitant procedures such as coronary artery bypass grafting (CABG) or aortic valve replacement (AVR) (Table 2). Patients undergoing ablation procedures experienced lower 30-day composite morbidity and mortality when compared with the other two groups (5.6% *vs.* 10.2% *vs.* 10%, $p = 0.011$), though there were no differences among groups comparing perioperative complications or 30 d rates of MI, stroke, or mortality (Table 2). There were no differences in long-term outcomes at 1 year postoperatively (Table 3).

Incidence of long-term outcomes including death, MI, and stroke/TIA are summarized in Table 4. After adjusting for significant covariates, surgical ablation remained an independent predictor of improved outcomes: patients who underwent ablation had a 62% lower long-term risk of stroke or TIA (0.38, 95% CI: 0.22–0.67, $p < 0.001$) and 20% lower long-term mortality risk (aHR 0.80, 95% CI: 0.66–0.95, $p = 0.012$), but no difference in risk of MI (aHR 0.67, 95% CI: 0.38–1.16, $p = 0.15$) (Table 5). LAAO was not associated with statistically significant differences in long-term risk of stroke or TIA, MI, death, or composite.

Discussion

This study demonstrated that in US veterans with AF undergoing MV surgery, surgical ablation for AF was inversely and independently associated with long-term stroke risk and long-term mortality, with no increased risk of perioperative complications. Isolated LAAO did not reduce long-term stroke risk or otherwise improve long-term outcomes for patients. These results join a growing body of evidence supporting the safety and efficacy of concomitant ablation at the time of MV surgery but questioning the utility of LAAO alone in this population.

Preoperative AF is common in patients undergoing MV surgery, with a prevalence of about 30% [20]. The addition of the Cox-maze procedure and other ablation techniques to MV surgery has been well established as safe [5,20,21], although it is not always offered to patients with high levels of surgical risk or comorbidities [21,22]. Randomized controlled trials have demonstrated that concomitant ablation reduces AF in patients undergoing MV surgery [23–25], and these benefits persist over time [26]. There is also evidence that ablation improves long-term survival for patients [27,28]. Some studies have demonstrated a decreased risk of stroke in patients after undergoing an ablation procedure for AF [6,26], while others have demonstrated no difference in the incidence of stroke or TIA in similar patient populations [29]. The 2017 Society of Thoracic Surgeons (STS) clinical practice guideline strongly recommends that ablation be performed at the time of MV surgery for patients with AF [5].

The present study supports the use of ablation for patients with pre-operative AF undergoing MV repair or replacement. It also demonstrates underutilization of ablation procedures in this patient population; only 50% of patients

Table 1. Patient Characteristics for Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery.

	No Ablation or LAAO (n = 458)	Ablation and LAAO (n = 645)	LAAO alone (n = 186)	*p*
Age (y)	68.1 ± 8.7	66.9 ± 8.0	70.1 ± 9.0	<0.001*
Sex (% male)	96.5	96.7	97.8	0.671
CHA_2DS_2-VASc Score	3.78 ± 1.5	3.53 ± 1.38	3.86 ± 1.46	0.003*
Renal failure (%)	3.7	3.3	2.2	0.6
ASA class				0.41
1	0.2	0	0	
2	0	0.2	0	
3	14.8	13.8	15.6	
4	84.9	85.7	83.3	
5	0	0.3	1.1	
Cardiomegaly (%)	54.4	44	49.5	0.003*
Cerebrovascular disease (%)	22.1	17.2	17.2	0.105
Heart failure (%)				<0.001*
None	2.9	1.4	4.3	
Class I	6.4	9.8	4.3	
Class II	25.2	28.5	30.3	
Class III	47.1	49.6	52.4	
Class IV	18.4	10.7	8.6	
COPD (%)	36.7	30.5	37.6	0.05*
CAD (%)				0.005*
None	53.3	65.3	59.2	
Mild	15.5	14.2	16.6	
Moderate	14.5	10.7	10.7	
Severe	16.7	9.8	13.6	
Smoking status (%)				0.821
Never smoker	21.2	24.2	26.3	
<14 days	16.4	14.7	14.5	
14 d–3 m	5.5	6	5.4	
>3 m	57	55	53.8	
Hypertension (%)	87.8	89.9	88.2	0.509
Diabetes (%)				0.369
No	74	76.9	72.6	
Diet	5.5	4.2	3.2	
Oral	10	11	11.5	
Insulin	10.5	7.9	12.4	
Prior PCI (%)	16	13	23.3	0.244
PVD (%)	15.9	8.4	12.4	<0.001*
Priority (%)				<0.001*
Elective	24.9	5.3	5.9	
Urgent/Emergent	75.1	94.7	94.1	
Prior MI (%)				0.903
No	88.3	87	85.6	
>7 d	11	12.2	13.8	
<7 d	0.7	0.8	0.6	
Prior Heart Surgery (%)	24.9	5.3	5.9	<0.001*

* $p < 0.05$ statistically significant. Abbreviations: ASA Class, American Society of Anesthesiologists Physical Classification; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; LAAO, left atrial appendage, occlusion; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease.

underwent ablation in comparison to approximately 60% reported in other studies [30] despite level 1A recommendation by the STS. This relative under-utilization is even more noteworthy given that patients with higher CHADS-VASC scores were less likely to receive concomitant ablation in the present study. This is a potential area of focus for qual-

Table 2. Operative Characteristics and Outcomes for Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery.

	No Ablation or LAAO (n = 458)	Ablation and LAAO (n = 645)	LAAO alone (n = 186)	*p*
CPB time (min)	178 ± 78	186 ± 64	182 ± 71	0.181
Ischemic time (min)	125 ± 63	133 ± 52	138 ± 61	0.018*
MVR (%)	55.4	38.5	59	<0.001*
CABG (%)	32.5	25.0	29.0	0.022*
AVR (%)	8.3	6.0	8.6	0.266
CABG and AVR (%)	4.8	2.9	4.3	0.263
Coma (%)	0.7	0.5	0.5	0.914
Mediastinitis (%)	0	0.5	0	0.223
Wound disruption (%)	0.3	0.4	0	0.424
Cardiac arrest (%)	5.5	6.8	4.3	0.374
Reop bleeding (%)	3.3	4.3	5.9	0.306
Reop CPB (%)	1.1	0.8	2.2	0.281
Operative mortality (%)	3.9	5.1	6.7	0.626
Vent 48 hr (%)	15.7	12.6	13.4	0.321
Reintubated w/in 30 d (%)	5.5	4	3.8	0.462
Tracheostomy (%)	3.7	2.8	2.7	0.644
ICU LOS (d)	7.7 ± 8.4	7.2 ± 7.7	7.5 ± 5.9	0.665
Hospital LOS (d)	13.3 ± 13	12.6 ± 7.8	12.8 ± 11.1	0.498
MI 30 d (%)	2.8	1.2	2.7	0.138
Stroke 30 d (%)	2.2	0.8	1.6	0.14
Mortality 30 d (%)	5	4.2	5.4	0.713
Composite 30 d (%)	10	5.6	10.2	0.011*

*$p < 0.05$ statistically significant. Abbreviations: AF, atrial fibrillation; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; LOS, length of stay; MI, myocardial infarction; MVR, mitral valve replacement; Reop, re-operative; Vent 48 hr, continued ventilation after 48 hours.

Table 3. Outcomes 1 Year Postoperatively for Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery.

	No Ablation or LAAO (n = 458)	Ablation and LAAO (n = 645)	LAAO alone (n = 186)	*p*
MI (%)	5	2.3	3.8	0.054
Stroke (%)	3.9	1.9	2.7	0.114
Mortality (%)	14.4	10.5	14	0.124
Composite (%)	19	14.3	19.4	0.066

Abbreviations: LAAO, left atrial appendage occlusion; MI, myocardial infarction.

Table 4. Incidence of Long-Term Surgical Outcomes for Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery.

Outcome	No Ablation or LAAO	Surgical Ablation and LAAO	LAAO alone	*p*
	(n = 458)	(n = 645)	(n = 186)	
Death n (%)	231 (50.4)	239 (37.1)	73 (39.2)	<0.001*
Stroke n (%)	34 (7.4)	20 (3.1)	9 (4.8)	0.005*
MI n (%)	30 (6.6)	26 (4.0)	16 (8.6)	0.031*
Composite n (%)	295 (64.4)	285 (44.2)	98 (52.7)	<0.001*

* $p < 0.05$ statistically significant. Abbreviations: LAAO, left atrial appendage occlusion; MI, myocardial infarction.

ity improvement in the VA and nationwide. Future research and quality improvement initiatives could include evaluating the data by region or by center and using the results to guide efforts to optimize patient outcomes.

Some studies have demonstrated long-term benefits of LAAO without ablation. In one retrospective cohort study, Yao *et al*. [31] demonstrated that LAAO was associated with decreased risk of stroke and all-cause mortality in patients with pre-operative AF undergoing CABG or valve surgery. In a separate multicenter randomized controlled trial including patients with AF undergoing cardiac surgery, Whitlock *et al*. [9] observed that patients who underwent concomitant LAAO had decreased risk of ischemic stroke when compared to patients who did not. Ando *et al*. [32]

Table 5. Long-term Surgical Outcomes for Patients with Atrial Fibrillation Undergoing Mitral Valve Surgery.

Intervention	Death			Stroke/TIA			MI			Composite		
	aHR	*p*	95% CI	aHR	*p*	95% CI	aHR	*p*	95% CI	aHR	*p*	95% CI
No Ablation or LAAO (reference) (n = 458)	1			1			1			1		
Surgical Ablation and LAAO	0.8	0.012	0.66–0.95	0.38	<0.001	0.22–0.67	0.67	0.15	0.38–1.16	0.75	0.001	0.63–0.89
LAAO alone	0.85	0.23	0.65–1.11	0.53	0.11	0.24–1.15	1.42	0.27	0.76–2.67	0.82	0.12	0.64–1.05

Results derived using a Cox proportional-hazards model. Adjusted hazard ratios (aHR) are reported for long-term outcomes along with 95% Confidence Interval (CI). Both treatment groups were compared to a reference group of patients undergoing mitral valve surgery without surgical ablation or left atrial appendage occlusion. Additional Abbreviations: LAAO, left atrial appendage occlusion; MI, myocardial infarction; TIA, transient ischemic attack.

performed a meta-analysis using 7 research articles including almost 3900 patients and observed that LAAO was associated with lower mortality and decreased risk of cerebral vascular accident (CVA) in patients with AF, while a meta-analysis by Tsai *et al*. [33] including 3653 patients showed decreased incidence of stroke and all-cause mortality in the LAAO group.

Two large retrospective cohort studies by Lee *et al*. [34] and Kim *et al*. [35] did not demonstrate long-term benefit of LAAO without ablation. The present study demonstrated a lower rate of long-term stroke within the group who underwent LAAO without ablation in comparison to the group that underwent neither ablation nor LAAO. However the adjusted hazard ratio was not statistically significant after adjusting for covariates. These data suggest LAAO without ablation does not confer as robust risk reduction as an ablation procedure, and does not support substitution of isolated LAAO in place of ablation with LAAO in patients with AF undergoing MV surgery.

Limitations

This study is subject to the inherent limitations of retrospective database research. Though the data within the database is collected prospectively, the retrospective nature of the study limits the extent to which variables can be controlled. Using available data, we were unable to differentiate permanent versus paroxysmal AF, which may have impacted surgeon decision-making to offer an ablation procedure as well as long-term outcomes. As noted in Table 1, our cohort populations had several differences in chronic medical conditions that are known risk factors for major morbidity, which may have affected our results despite best efforts to implement multivariable statistical controls. Additionally, as it is true for all the studies performed within the VA system, most included patients are male, limiting the generalizability of the results.

Our study is limited by several absent post-operative data points, including postoperative use of anticoagulation which could have affected stroke outcomes. We also lack data on postoperative rhythm conversion to sinus or reversion to AF, as well as the post-operative need for pacemaker, a known complication of ablation procedures.

This study is limited by the smaller number of patients undergoing LAAO and these results should be interpreted accordingly. While the adjusted hazard ratio for stroke did not reach statistical significance, there was a lower rate of strokes with LAAO when compared to no ablation or LAAO, and it is possible that with a larger sample size or longer follow-up these differences may have reached significance.

There is potential for selection bias in our study, as it included data only from patients who eventually received some type of major surgical intervention. There is inherent selection bias by surgeons, who may choose not to offer ablation or LAAO to older or more chronically ill patients due to concerns of increased short-term morbidity or prolonged cardiopulmonary bypass time. Finally, surgeons with greater experience and expertise are possibly more likely to offer concomitant ablation.

Conclusions

In veterans with AF undergoing MV surgery, surgical ablation for AF was inversely and independently associated with long-term stroke risk and long-term mortality, with no increased risk of perioperative complications. Isolated LAAO did not reduce long-term stroke risk. These results support the continued role of ablation procedures in the treatment of AF at the time of MV surgery and highlight the need for randomized controlled trials. This study also suggests that ablation for atrial fibrillation is underutilized in the Veterans Health Administration and may be a target of future quality improvement efforts.

Abbreviations

AF, atrial fibrillation; AVR, Aortic Valve Replacement; CABG, Coronoary Artery Bypass Graft; CAD, Coronary Artery Disease; CDW, Corporate Data Warehouse; LAAO, left atrial appendage occlusion; MI, myocardial infarction; MV, mitral valve; STS, Society of Thoracic Surgeons; TIA, Transient Ischemic Attack; VASQIP, Veterans Affairs Surgical Quality Improvement Program; VHA, Veterans Health Administration; VINCI, Veterans Affairs Informatics and Computing Infrastructure.

Availability of Data and Materials

Data and materials are available through direct request to the corresponding author.

Author Contributions

JD, JA, and GDT designed the research study. JD performed the research. JD, SH and AP analyzed the data, wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Institutional review board approval and a waiver of informed consent was obtained from the Washington, D.C. VA Medical Center. This study was conducted under the supervision of the Washington, D.C. Veterans Affairs Medical Center IRB, IRBNet ID 1584919-3, initially approved 12/2/2011.

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Conflict of Interest

The authors declare no conflict of interest. GDT is a member of the editorial board of this journal. GDT declares that he was not involved in the processing of this article and has no access to information regarding its processing.

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