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Association of Surgical Left Atrial Appendage Occlusion With Subsequent Stroke and Mortality Among Patients Undergoing Cardiac Surgery

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IMPORTANCE Surgical occlusion of the left atrial appendage (LAAO) may be performed during concurrent cardiac surgery. However, few data exist on the association of LAAO with long-term risk of stroke, and some evidence suggests that this procedure may be associated with subsequent development of atrial fibrillation (AF).

OBJECTIVE To evaluate the association of surgical LAAO performed during cardiac surgery with risk of stroke, mortality, and development of subsequent AF.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study using a large US administrative database that contains data from adult patients (≥18 years) with private insurance or Medicare Advantage who underwent coronary artery bypass graft (CABG) or valve surgery between January 1, 2009, and March 30, 2017, with final follow-up on March 31, 2017. One-to-one propensity score matching was used to balance patients on 76 dimensions to compare those with vs without LAAO, stratified by history of prior AF at the time of surgery.

EXPOSURES Surgical LAAO vs no surgical LAAO during cardiac surgery.

MAIN OUTCOMES AND MEASURES The primary outcomes were stroke (ie, ischemic stroke or systemic embolism) and all-cause mortality. The secondary outcomes were postoperative AF (AF within 30 days after surgery among patients without prior AF) and long-term AF-related health utilization (event rates of outpatient visits and hospitalizations).

RESULTS Among 75 782 patients who underwent cardiac surgery (mean age, 66.0 [SD, 11.2] years; 2 2091 [29.2%] women, 25 721 [33.9%] with preexisting AF), 4374 (5.8%) underwent concurrent LAAO, and mean follow-up was 2.1 (SD, 1.9) years. In the 8590 propensity score–matched patients, LAAO was associated with a reduced risk of stroke (1.14 vs 1.59 events per 100 person-years; hazard ratio [HR], 0.73 [95% CI, 0.56-0.96]; $P = .03$) and mortality (3.01 vs 4.30 events per 100 person-years; HR, 0.71 [95% CI, 0.60-0.84]; $P < .001$). LAAO was associated with higher rates of AF-related outpatient visits (11.96 vs 10.26 events per person-year; absolute difference, 1.70 [95% CI, 1.60-1.80] events per person-year; rate ratio, 1.17 [95% CI, 1.10-1.24]; $P < .001$) and hospitalizations (0.36 vs 0.32 event per person-year; absolute difference, 0.04 [95% CI, 0.02-0.06] event per person-year; rate ratio, 1.13 [95% CI, 1.05-1.21]; $P = .002$). In patients with prior AF (6438/8590 [74.9%]) with vs without LAAO, risk of stroke was 1.11 vs 1.71 events per 100 person-years (HR, 0.68 [95% CI, 0.50-0.92]; $P = .01$) and risk of mortality was 3.22 vs 4.93 events per 100 person-years (HR, 0.67 [95% CI, 0.56-0.80]; $P < .001$), respectively. In patients without prior AF (2152/8590 [25.1%]) with vs without LAAO, risk of stroke was 1.23 vs 1.26 events per 100 person-years (HR, 0.95 [95% CI, 0.54-1.68]), risk of mortality was 2.30 vs 2.49 events per 100 person-years (HR, 0.92 [95% CI, 0.61-1.37]), and risk of postoperative AF was 27.7% vs 20.2% events per 100 person-years (HR, 1.46 [95% CI, 1.22-1.73]; $P < .001$). The interaction term between prior AF and LAAO was not significant ($P = .29$ for stroke and $P = .16$ for mortality).

CONCLUSIONS AND RELEVANCE Among patients undergoing cardiac surgery, concurrent surgical LAAO, compared with no surgical LAAO, was associated with reduced risk of subsequent stroke and all-cause mortality. Further research, including from randomized clinical trials, is needed to more definitively determine the role of surgical LAAO.

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Supplemental content

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Cardiac surgery is among the most commonly performed procedures, with more than 300 000 coronary artery bypass graft (CABG) and valve operations performed annually in the United States.[1] Many patients who undergo cardiac surgery have a history of atrial fibrillation (AF), which is associated with an increased risk of stroke.[2,3] Because thrombi in the left atrial appendage may account for the majority of cardioembolic strokes in AF,[4] surgical occlusion of the left atrial appendage (LAAO) is sometimes performed during the surgery to reduce long-term risk of stroke.

There are limited data on the effectiveness of LAAO to guide evidence-based decision making. A recent observational study demonstrated that LAAO was associated with a lower risk of thromboembolism in patients with AF.[5] However, LAAO may not be beneficial in patients without AF, but in another recent observational study, more than half of the patients undergoing LAAO did not have prior AF, perhaps indicating that preemptive closure in patients perceived to be at a high risk of developing AF is common practice.[6] However, little is known whether this approach is justified. Therefore, this study aimed to investigate whether LAAO during cardiac surgery was associated with reduced risks of stroke and mortality. This study specifically assessed outcomes stratified by whether patients had a history of AF at the time of surgery.

A secondary aim was to investigate whether LAAO was associated with subsequent AF. A previous study found that LAAO may be associated with increased risk of postoperative AF,[6] perhaps by promoting an atrial arrhythmogenic state resulting from increased left atrial filling pressures, inflammation, and sympatho-vagal imbalance.[7-9] As such, this study examined the association between LAAO and postoperative AF, as well as long-term AF-related health care utilization.

Key Points

Question Is surgical occlusion of the left atrial appendage (LAAO) during cardiac surgery associated with reduced risk of stroke or all-cause mortality?

Finding In this retrospective cohort study of 75 782 patients undergoing cardiac surgery, concurrent surgical LAAO, compared with no surgical LAAO, was significantly associated with a lower risk of stroke (hazard ratio, 0.73) and mortality (hazard ratio, 0.71) among a propensity score–matched cohort of 8590 patients.

Meaning Surgical LAAO in patients undergoing concurrent cardiac surgery was associated with reduced risk of subsequent stroke and all-cause mortality.

Methods

The Mayo Clinic institutional review board exempted this study from review because the study used preexisting, deidentified data.

Study Population

This study was a retrospective cohort analysis using OptumLabs Data Warehouse, which contains data from patients with private insurance or Medicare Advantage of all ages and races throughout the United States.[10,11] The cohort included adult patients (≥18 years) who underwent their first CABG or valve surgery (open-heart valve replacement or repair) between January 1, 2009, and March 30, 2017. Patients were required to have at least 6 months of continuous enrollment in health insurance plans before the the surgery, defined as the baseline period, to capture patients' medical history. The mean baseline period was 3.8 (SD, 3.3) years.

The variables were defined by the presence of a claim with eligible diagnosis codes, procedure codes, or prescription fills. The absence of such claims was interpreted as the absence of the condition. Race/ethnicity was measured because it is a major socioeconomic characteristic and a risk factor for outcomes. The data were provided by OptumLabs, classified as non-Hispanic white (white), non-Hispanic black (black), Asian, Hispanic, or other/unknown. Self-report was the primary source, and when data were missing, imputation was made by the data provider based on other available administrative data.[12]

Exposure

LAAO was identified using *International Classification of Diseases, Ninth Revision* (*ICD-9*) and *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) procedure codes (*ICD-9* 37.36; *ICD-10* 02570ZK, 02B70ZK, 02L70ZK, 02L70CK).

Outcomes

The primary outcomes were ischemic stroke or systemic embolism (hereafter referred to as stroke) and all-cause mortality. Stroke was defined as a primary diagnosis during an emergency department visit or a primary or secondary diagnosis during an inpatient stay (diagnosis codes for stroke: *ICD-9* 433.x1, 434.x1, 436, and 444.x; *ICD-10* I63.x, I74.x). Mortality was identified based on the Social Security Death Master File and discharge status.

The secondary outcomes were postoperative AF, defined as newly diagnosed AF within 30 days after the surgery (a diagnosis code on an inpatient or outpatient claim [*ICD-9* 427.31; *ICD-10* I48.0, I48.1, I48.2, I48.91]), and long-term AF-related health utilization, measured by the event rates of outpatient visits and hospitalizations with a diagnosis of AF. Although AF-related health utilization may underestimate the occurrence and frequency of AF episodes, it could be considered as a surrogate measure of the effect of AF on patients' health and quality of life, as well as the burden on the health care system.

Follow-up started from the day after the surgery until the end of the study period (March 31, 2017), the end of enrollment in health insurance plans, or death, whichever happened first. All outcomes were compared in the entire cohort, except for postoperative AF, which was assessed only in patients without prior AF, to avoid misclassification of "carry forward" diagnoses as postoperative AF episodes.

Statistical Analysis

The statistical analysis plan is available in Supplement 1. Propensity score matching was used to balance the differences in baseline characteristics between patients who underwent concurrent LAAO and those who did not. A propensity score, the probability of undergoing LAAO, was estimated using logistic regression based on sociodemographic characteristics, procedure-related

characteristics, medical history, concurrent medication use, year of the surgery, and the length of baseline period. Baseline medication use was defined as prescriptions within 3 months of the surgery, and the preoperative medication was defined as prescription within 1 week of the surgery. One-to-one nearest-neighbor caliper matching was used to match patients based on the logit of the propensity score using a caliper equal to 0.2 of the standard deviation of the logit of the propensity score.[13] Patients were exact matched on baseline AF and use of oral anticoagulation.

Standardized difference was used to assess the balance of covariates after matching, and a standardized difference less than 10% was considered acceptable.[14] Balance of baseline characteristics was also assessed in patients with and without prior AF separately, because the comparisons between patients treated with and without LAAO were stratified by the presence of prior AF. Whether the hazard ratios (HRs) were the same between patients with and without prior AF was tested by the significance of the interaction term. One-third of the cohort had linked blood-based laboratory results. The availability of laboratory data depended on the contract between laboratory testing facilities and OptumLabs, rather than individual patient characteristics. Laboratory data were used to assess values for serum creatinine, serum calcium, serum albumin, hemoglobin, low-density lipoprotein cholesterol, and hemoglobin A_{1c}. These laboratory data were not included in the model to calculate the propensity score, but the values and the proportion of missing values were balanced after matching on all other patient characteristics.

Cox proportional hazards regression was used to compare patients treated with and without LAAO for stroke, mortality, and postoperative AF in the propensity score–matched cohort, with robust sandwich estimates to account for the clustering within matched sets.[15] The Fine and Gray method was used to consider death as a competing risk when assessing nonfatal outcomes.[16] The proportional hazards assumption was tested on the basis of Schoenfeld residuals.[17] Poisson regression was used to assess AF-related outpatient visits and hospitalizations.

$P < .05$ was considered statistically significant for all tests. All tests were 2-sided. All analyses were conducted using SAS version 9.4 (SAS Institute Inc) and Stata version 14.1 (StataCorp).

Sensitivity Analyses

Subgroup analyses for stroke and mortality were performed stratified by age, sex, race, surgery types, CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes, stroke/transient ischemic attack/thromboembolism [doubled], vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]), HAS-BLED score (hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly, drugs or alcohol), prior thromboembolism, prior bleeding, heart failure, and stage 3-5 chronic kidney disease. Whether the HRs were the same across the subgroups was tested by the significance of the interaction terms.

Analyses using falsification end points were performed to test for residual confounding.[18] Three end points unlikely to be a result of undergoing LAAO were selected: chronic obstructive pulmonary disease, pneumonia, and fracture.

Sensitivity analyses were conducted using propensity score weighting (an overlap weight) instead of matching.[19] Another sensitivity analysis was conducted assessing outcomes by the use of oral anticoagulants during follow-up. In patients without prior AF, a sensitivity analysis was conducted for stroke and mortality, stratified by whether patients developed AF during follow-up. AF-related health utilization excluding the first 30 days, stratified by whether patients had postoperative AF, was examined to assess whether patients with postoperative AF developed late AF.

To illustrate variables associated with LAAO, multivariable logistic regression was performed in the entire cohort. To illustrate variables associated with postoperative AF, multivariable Cox proportional hazards regression was performed in patients without prior AF. In these 2 multivariable regression models, independent variables were selected using stepwise forward selection using a threshold of $P = .10$ for the addition to the model. A sensitivity analysis was performed in patients with prior AF, adjusting for whether patients underwent concomitant Maze procedure. All sensitivity and subgroup analyses were prespecified but were considered exploratory.

Results

Patient Characteristics

Among 75 782 patients who underwent cardiac surgery, the mean age was 66.0 (SD, 11.2) years; 22 091 (29.2%) were women, 67 410 (89.0%) had a CHA_2DS_2-VASc score of 2 or more, 25 721 (33.9%) had preexisting AF, and 4374 (5.8%) underwent concurrent LAAO. Variables significantly associated with undergoing LAAO included a history of AF, valve surgery (particularly valve repair and mitral valve surgery), the use of oral anticoagulants before the surgery, and surgery performed in more recent years (eTable 1 in Supplement 2).

The propensity score–matched cohort included 8590 patients followed up for a mean of 2.1 (SD, 1.9) years. Patients treated with and without LAAO were balanced on 76 baseline characteristics (**Table 1** and **Table 2**). Of these patients, 2152/8590 (25.1%) did not have a history of AF; baseline characteristics stratified by whether patients had prior AF are reported in eTable 2 in Supplement 2. In patients with prior AF, the baseline characteristics were all balanced between patients who underwent LAAO and those who did not. In patients without prior AF, because of a relatively small number of patients, several variables had some imbalance, but adjusting for these variables in the regression analyses did not change the results.

Primary and Secondary Outcomes

Overall in the propensity score–matched patients, LAAO was associated with a reduced risk of stroke (1.14 vs 1.59 events per 100 person-years; absolute difference, 0.45 [95% CI, 0.09 to 0.82] event per 100 person-years; HR, 0.73 [95% CI, 0.56 to 0.96]; $P = .03$) and mortality (3.01 vs 4.30 events per 100 person-years; absolute difference, 1.29 [95% CI, 0.70 to 1.89] events per 100 person-years; HR, 0.71 [95% CI, 0.60 to 0.84]; $P < .001$) (**Table 3** and **Figure 1**). The proportional hazards assumption was valid for all outcomes.

Table 1. Baseline Demographic Characteristics and Medical History Before and After Propensity Score Matching

Characteristic	Before Propensity Score Matching		After Propensity Score Matching		
	No LAAO, No. (%) (n = 71 408)	LAAO, No. (%) (n = 4374)	No LAAO, No. (%) (n = 4295)	LAAO, No. (%) (n = 4295)	Standardized Difference, %
Age, y	65.8 (11.3)	68.2 (10.6)	68.4 (10.8)	68.2 (10.6)	1.5
18-64	30 157 (42.2)	1471 (33.6)	1431 (33.3)	1442 (33.6)	0.5
65-74	24 265 (34.0)	1528 (34.9)	1461 (34.0)	1497 (34.9)	1.8
≥75	16 986 (23.8)	1375 (31.4)	1403 (32.7)	1356 (31.6)	2.3
Women	20 553 (28.8)	1538 (35.2)	1515 (35.3)	1506 (35.1)	0.4
Race					
Asian	1485 (2.1)	64 (1.5)	59 (1.4)	64 (1.5)	1.0
Black	6171 (8.6)	307 (7.0)	296 (6.9)	305 (7.1)	0.8
Hispanic/Latino	4310 (6.0)	177 (4.0)	175 (4.1)	175 (4.1)	0.0
White	54 863 (76.8)	3486 (79.7)	3424 (79.7)	3421 (79.7)	0.2
Other/unknown	4579 (6.4)	340 (7.8)	341 (7.9)	330 (7.7)	1.0
Geographic region					
Midwest	22 613 (31.7)	1755 (40.1)	1723 (40.1)	1710 (39.8)	0.6
Northeast	9500 (13.3)	497 (11.4)	500 (11.6)	497 (11.6)	0.2
South	32 436 (45.4)	1527 (34.9)	1495 (34.8)	1516 (35.3)	1.0
West	6859 (9.6)	595 (13.6)	577 (13.4)	572 (13.3)	0.3
Medical history					
Atrial fibrillation	22 423 (31.4)	3298 (75.4)	3219 (74.9)	3219 (74.9)	0.0
Other supraventricular arrhythmia	20 035 (28.1)	2190 (50.1)	2161 (50.3)	2122 (49.4)	1.8
Thromboembolism	12 038 (16.9)	775 (17.7)	806 (18.8)	768 (17.9)	2.3
Heart failure	28 182 (39.5)	2422 (55.4)	2402 (55.9)	2367 (55.1)	1.6
Diabetes mellitus	31 651 (44.3)	1523 (34.8)	1539 (35.8)	1508 (35.1)	1.5
Stage 3-5 CKD	9345 (13.1)	600 (13.7)	603 (14.0)	595 (13.9)	0.5
Myocardial infarction	29 481 (41.3)	1102 (25.2)	1112 (25.9)	1098 (25.6)	0.7
Peripheral artery disease	12 530 (17.5)	586 (13.4)	596 (13.9)	586 (13.6)	0.7
Major bleeding	13 976 (19.6)	1066 (24.4)	1052 (24.5)	1045 (24.3)	0.4
Intracranial bleeding	928 (1.3)	89 (2.0)	83 (1.9)	87 (2.0)	0.7
Hypertension	64 537 (90.4)	3874 (88.6)	3803 (88.5)	3807 (88.6)	0.3
Hyperlipidemia	63 313 (88.7)	3686 (84.3)	3676 (85.6)	3629 (84.5)	3.1
Falls	6006 (8.4)	441 (10.1)	432 (10.1)	430 (10.0)	0.2
Anemia	46 228 (64.7)	3178 (72.7)	3161 (73.6)	3119 (72.6)	2.2
COPD	8914 (12.5)	584 (13.4)	563 (13.1)	578 (13.5)	1.0
Alcoholism	3688 (5.2)	271 (6.2)	271 (6.3)	263 (6.1)	0.8
Obesity	20 785 (29.1)	1235 (28.2)	1207 (28.1)	1213 (28.2)	0.3
Smoking	30 554 (42.8)	1647 (37.7)	1585 (36.9)	1627 (37.9)	2.0
Obstructive sleep apnea	12 389 (17.3)	921 (21.1)	923 (21.5)	896 (20.9)	1.5
Nonskin cancer	10 089 (14.1)	683 (15.6)	662 (15.4)	672 (15.6)	0.6
Ischemic stroke or systemic embolism	9266 (13.0)	580 (13.3)	617 (14.4)	575 (13.4)	2.8
Transient ischemic attack	5705 (8.0)	404 (9.2)	426 (9.9)	398 (9.3)	2.2
Ventricular arrhythmia	8502 (11.9)	767 (17.5)	750 (17.5)	749 (17.4)	0.1
Systolic heart failure	12 015 (16.8)	1114 (25.5)	1126 (26.2)	1078 (25.1)	2.6
Diabetes requiring insulin	9115 (12.8)	368 (8.4)	363 (8.5)	365 (8.5)	0.2
Dialysis	1626 (2.3)	67 (1.5)	69 (1.6)	67 (1.6)	0.4
Cardioversion	2145 (3.0)	680 (15.5)	604 (14.1)	622 (14.5)	1.2
Ablation	673 (0.9)	187 (4.3)	167 (3.9)	174 (4.1)	0.8
Pacemaker or ICD	5269 (7.4)	567 (13.0)	580 (13.5)	556 (12.9)	1.6
PCI	9474 (13.3)	354 (8.1)	344 (8.0)	351 (8.2)	0.6
Liver disease	9262 (13.0)	579 (13.2)	563 (13.1)	569 (13.2)	0.4
Depression	22 088 (30.9)	1385 (31.7)	1375 (32.0)	1358 (31.6)	0.8
Dementia	1832 (2.6)	129 (2.9)	130 (3.0)	127 (3.0)	0.4
Hypothyroidism	14 826 (20.8)	1041 (23.8)	1053 (24.5)	1019 (23.7)	1.9
Thyrotoxicosis	2134 (3.0)	191 (4.4)	189 (4.4)	185 (4.3)	0.5
Ulcer in upper GI tract	3688 (5.2)	232 (5.3)	244 (5.7)	229 (5.3)	1.5
Preoperative endocarditis	786 (1.1)	71 (1.6)	81 (1.9)	71 (1.7)	1.8

(continued)

Table 1. Baseline Demographic Characteristics and Medical History Before and After Propensity Score Matching (continued)

Characteristic	Before Propensity Score Matching		After Propensity Score Matching		
	No LAAO, No. (%) (n = 71 408)	LAAO, No. (%) (n = 4374)	No LAAO, No. (%) (n = 4295)	LAAO, No. (%) (n = 4295)	Standardized Difference, %
CHA_2DS_2-VASc score[a]					
0, 1	7901 (11.1)	471 (10.8)	457 (10.6)	460 (10.7)	0.2
2, 3	26 982 (37.8)	1515 (34.6)	1398 (32.5)	1482 (34.5)	4.1
≥4	36 525 (51.1)	2388 (54.6)	2440 (56.8)	2353 (54.8)	4.1
HAS-BLED score ≥3[b]	42 278 (59.2)	2782 (63.6)	2808 (65.4)	2733 (63.6)	3.6
Baseline medication					
Oral anticoagulant	4393 (6.2)	1368 (31.3)	1308 (30.5)	1308 (30.5)	0.0
Antiplatelet	9834 (13.8)	327 (7.5)	313 (7.3)	327 (7.6)	1.2
Rate-control drugs	32 320 (45.3)	2455 (56.1)	2411 (56.1)	2389 (55.6)	1.0
Antiarrhythmic drugs	2302 (3.2)	601 (13.7)	539 (12.5)	546 (12.7)	0.5
Other adrenergic blocking agents	3798 (5.3)	206 (4.7)	206 (4.8)	204 (4.7)	0.2
Other calcium channel blockers	11 372 (15.9)	575 (13.1)	570 (13.3)	571 (13.3)	0.1
Renin-angiotensin system antagonists	30 801 (43.1)	1896 (43.3)	1875 (43.7)	1863 (43.4)	0.6
Loop diuretics	9270 (13.0)	1165 (26.6)	1108 (25.8)	1126 (26.2)	1.0
Thiazides	11 382 (15.9)	627 (14.3)	598 (13.9)	623 (14.5)	1.7
Cholesterol-lowering drugs	34 414 (48.2)	2009 (45.9)	1998 (46.5)	1979 (46.1)	0.9
NSAIDs	7008 (9.8)	372 (8.5)	377 (8.8)	359 (8.4)	1.5
Diabetes drugs	13 483 (18.9)	552 (12.6)	575 (13.4)	547 (12.7)	1.9
Antiulcer agents	13 144 (18.4)	826 (18.9)	815 (19.0)	811 (18.9)	0.2
Preoperative medication					
β-Blocker	6115 (8.6)	345 (7.9)	369 (8.6)	340 (7.9)	2.5
Amiodarone	573 (0.8)	79 (1.8)	72 (1.7)	74 (1.7)	0.4
Statin	5404 (7.6)	290 (6.6)	263 (6.1)	288 (6.7)	2.4
Corticosteroid	1492 (2.1)	81 (1.9)	100 (2.3)	81 (1.9)	3.1
Laboratory results, mean (SD)					
Serum creatinine, mg/dL	1.2 (2.9)	1.1 (0.5)	1.1 (0.4)	1.1 (0.5)	6.6
Serum calcium, mg/dL	9.4 (0.5)	9.4 (0.5)	9.4 (0.5)	9.4 (0.5)	2.2
Serum albumin, g/dL	4.2 (0.4)	4.2 (0.4)	4.2 (0.4)	4.2 (0.4)	2.7
Hemoglobin, g/dL	13.7 (1.8)	13.5 (1.8)	13.4 (1.8)	13.5 (1.8)	7.7
LDL-C, mg/dL	104.0 (39.6)	97.6 (35.6)	96.0 (34.9)	97.5 (35.6)	4.3
HbA_{1c}, %	7.1 (1.7)	6.7 (1.4)	6.7 (1.5)	6.7 (1.4)	0.7

Abbreviations: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HbA_{1c}, hemoglobin A_{1c}; ICD, implantable cardioverter-defibrillator; LAAO, surgical occlusion of the left atrial appendage; LDL-C, low-density lipoprotein cholesterol; NSAID, nonsteroidal anti-inflammatory drug; PCI, percutaneous coronary intervention.

SI conversion factors: To convert creatinine values to μmol/L, multiply by 88.4; calcium values to mmol/L, multiply by 0.25; LDL-C values to mmol/L, multiply by 0.0259.

[a] Range, 0 to 9; higher score indicates higher risk of stroke. Point score is calculated as 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex; 2 points for 75 years or older and prior stroke, TIA, or thromboembolism.

[b] Range, 0 to 9; higher score indicates higher risk of bleeding. Point score is calculated as 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio (INR), older than 65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider INR, so the range is 0 to 8.

LAAO was associated with higher rates of AF-related outpatient visits (11.96 vs 10.26 events per person-year; absolute difference, 1.70 [95% CI, 1.60 to 1.80] events per person-year; rate ratio, 1.17 [95% CI, 1.10 to 1.24]; $P < .001$) and hospitalizations (0.36 vs 0.32 event per person-year; absolute difference, 0.04 [95% CI, 0.02 to 0.06] event per person-year; rate ratio, 1.13 [95% CI, 1.05 to 1.21]; $P = .002$) (**Table 4**).

Stratified Analyses by Preexisting AF

Among the 6438 patients with prior AF in the matched cohort, for those with LAAO vs no LAAO, the risk of stroke was 1.11 vs 1.71 events per 100 person-years, respectively (absolute difference, 0.60 [95% CI, 0.16 to 1.03] event per 100 person-years; HR, 0.68 [95% CI, 0.50 to 0.92]; $P = .01$), and the risk of mortality was 3.22 vs 4.93 events per 100 person-years (absolute difference, 1.70 [95% CI, 0.98 to 2.43] events per 100 person-years; HR, 0.67 [95% CI, 0.56 to 0.80]; $P < .001$). Among the 2152 patients without prior AF for those with vs without LAAO, the risk of stroke was 1.23 vs 1.26 events per 100 person-years, respectively (absolute difference, 0.04 [95% CI, −0.67 to 0.74] event per 100 person-years; HR, 0.95 [95% CI, 0.54 to 1.68]), and the risk of mortality was 2.30 vs 2.49 events per 100 person-years (absolute difference, 0.19 [95% CI, −0.78 to 1.16] event per 100 person-years; HR, 0.92 [95% CI, 0.61 to 1.37](Table 3 and Figure 1). The interaction term between prior AF and LAAO was not statistically significant ($P = .29$ for stroke and $P = .16$ for mortality).

Table 2. Procedure-Related Characteristics Before and After Propensity Score Matching

Characteristic	Before Propensity Score Matching		After Propensity Score Matching		
	No LAAO, No. (%) (n = 71 408)	LAAO, No. (%) (n = 4374)	No LAAO, No. (%) (n = 4295)	LAAO, No. (%) (n = 4295)	Standardized Difference, %
Surgery types					
CABG	54 206 (75.9)	2012 (46.0)	1924 (44.8)	2006 (46.7)	3.8
Mechanical valve replacement	6006 (8.4)	386 (8.8)	408 (9.5)	386 (9.0)	1.8
Bioprosthetic valve replacement	14 405 (20.2)	1506 (34.4)	1531 (35.6)	1493 (34.8)	1.9
Valve repair	5134 (7.2)	1227 (28.1)	1183 (27.5)	1161 (27.0)	1.1
CABG + valve surgery	8343 (11.7)	757 (17.3)	751 (17.5)	751 (17.5)	0.0
Valves treated during valve surgery[a]					
Aortic	17 697 (69.3)	1174 (37.6)	1251 (40.1)	1173 (38.6)	3.0
Mitral	7276 (28.5)	1946 (62.4)	1871 (59.9)	1867 (61.4)	3.0
Tricuspid or pulmonary	2125 (8.3)	451 (14.5)	422 (13.5)	432 (14.2)	2.0
Both mitral and aortic valves	636 (2.5)	121 (3.9)	133 (4.3)	120 (3.9)	
On-pump surgery	48 723 (68.2)	3467 (79.3)	3388 (78.9)	3390 (78.9)	0.1
Preoperative hemodynamic instability[b]	731 (1.0)	25 (0.6)	30 (0.7)	25 (0.6)	1.5
Year of index procedure					
2009	7922 (11.1)	230 (5.3)	263 (6.1)	230 (5.4)	3.3
2010	7910 (11.1)	326 (7.5)	310 (7.2)	326 (7.6)	1.4
2011	8028 (11.2)	347 (7.9)	338 (7.9)	347 (8.1)	0.8
2012	8372 (11.7)	412 (9.4)	402 (9.4)	411 (9.6)	0.7
2013	9078 (12.7)	593 (13.6)	600 (14.0)	587 (13.7)	0.9
2014	8278 (11.6)	599 (13.7)	568 (13.2)	590 (13.7)	1.5
2015	8751 (12.3)	754 (17.2)	759 (17.7)	731 (17.0)	1.7
2016	10 322 (14.5)	887 (20.3)	859 (20.0)	855 (19.9)	0.2
2017	2747 (3.8)	226 (5.2)	196 (4.6)	218 (5.1)	2.4
Length of baseline period, y[c]	3.7 (3.3)	3.9 (3.3)	3.9 (3.3)	3.9 (3.3)	0.8

Abbreviations: CABG, coronary artery bypass graft; LAAO, surgical occlusion of the left atrial appendage.

[a] Proportions calculated among patients who underwent valve surgery.

[b] Includes cardiogenic shock, cardiac arrest, and resuscitation within 1 week before the procedure.

[c] Time period before the surgery, which was used to establish patients' medical history. Concomitant Maze procedure was performed in 2196 of the patients (2.9%), including 1068 (24.4%) of patients who underwent LAAO and 1128 (1.6%) of patients who did not undergo LAAO.

Table 3. Stroke and All-Cause Mortality in Propensity Score–Matched Patients

Outcome	No LAAO				LAAO				Absolute Rate Difference (95% CI)[a]	HR (95% CI)	*P* Value[b]
	No. of Patients	No. of Events	Person-Years	Event Rate[a]	No. of Patients	No. of Events	Person-Years	Event Rate[a]			
Ischemic Stroke or Systemic Embolism											
Overall	4295	122	7665	1.59	4295	90	7908	1.14	0.45 (0.09 to 0.82)	0.73 (0.56 to 0.96)	.03
AF at baseline	3219	97	5683	1.71	3219	67	6032	1.11	0.60 (0.16 to 1.03)	0.68 (0.50 to 0.92)	.01
No AF at baseline	1076	25	1982	1.26	1076	23	1877	1.23	0.04 (−0.67 to 0.74)	0.95 (0.54 to 1.68)	.87
Death											
Overall	4295	335	7792	4.30	4295	243	8083	3.01	1.29 (0.70 to 1.89)	0.71 (0.60 to 0.84)	<.001
AF at baseline	3219	285	5782	4.93	3219	199	6171	3.22	1.70 (0.98 to 2.43)	0.67 (0.56 to 0.80)	<.001
No AF at baseline	1076	50	2010	2.49	1076	44	1912	2.30	0.19 (−0.78 to 1.16)	0.92 (0.61 to 1.37)	.67

Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage.

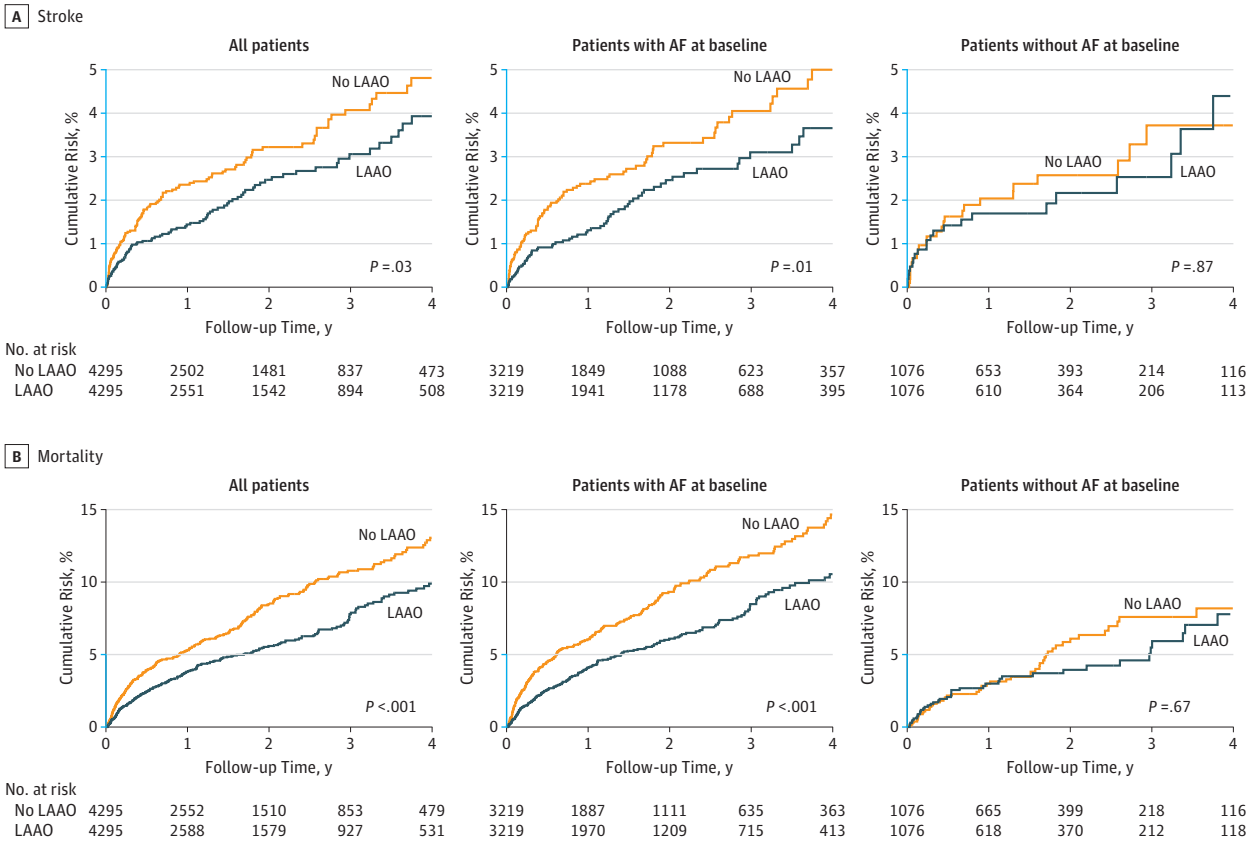
[a] Calculated as the number of events per 100 person-years.

[b] The interaction term between prior AF and LAAO was not statistically significant (*P* = .29 for stroke and *P* = .16 for mortality).

Among the 2152 patients without prior AF in the matched cohort, 515 (23.9%) developed newly diagnosed AF within 30 days after surgery. LAAO vs no LAAO was associated with a higher risk of postoperative AF (27.7% vs 20.2%; HR, 1.46 [95% CI, 1.22 to 1.73]; *P* < .001).

In the propensity score–matched patients with prior AF with LAAO vs without LAAO, rates were 14.74 vs 13.11 events per person-year, respectively (absolute difference, 1.62 [95% CI, 1.49 to 1.76] events per person-year; rate ratio, 1.12 [95% CI, 1.06 to 1.19]; *P* < .001), for AF-related outpatient visits and 0.44 vs 0.41 event per person-year (absolute difference, 0.04 [95% CI, 0.01 to 0.06] event per person-year; rate ratio, 1.09 [95% CI, 1.01 to 1.17]; *P* = .03) for hospitalizations. Among patients without prior AF with LAAO vs without LAAO, rates were 3.01 vs 2.05 events per person-year, respectively (absolute difference, 0.95 [95% CI, 0.85 to 1.05] event per person-year; rate ratio, 1.46 [95% CI, 1.10 to 1.96]; *P* = .01), for outpatient visits and 0.08 vs 0.06 event per person-year (absolute difference,

Figure 1. Cumulative Risks of Stroke and All-Cause Mortality in Propensity Score–Matched Patients



Y-axis scale in blue indicates range from 0% to 5%. All reported *P* values were obtained from Cox proportional hazards models. For stroke, in the surgical occlusion of the left atrial appendage (LAAO) group, median follow-up times were 1.4 (interquartile range [IQR], 0.5-2.7) years for all patients, 1.4 (IQR, 0.6-2.7) years for patients with prior atrial fibrillation (AF), and 1.2 (IQR, 0.5-2.6) years for patients without prior AF; in the no LAAO group, median follow-up times were 1.3 (IQR, 0.5-2.6) years for all patients, 1.3 (IQR, 0.5-2.5) years for patients with prior AF, and 1.4 (IQR, 0.5-2.7) years for patients without prior AF. For mortality, in the LAAO group, median follow-up times were 1.4 (IQR, 0.6-2.8) years for all patients, 1.5 (IQR, 0.6-2.8) years for patients with prior AF, and 1.2 (IQR, 0.5-2.6) years for patients without prior AF; in the no LAAO group, median follow-up times were 1.4 (IQR, 0.6-2.6) years for all patients, 1.3 (IQR, 0.6-2.5) years for patients with prior AF, and 1.5 (IQR, 0.6-2.7) years for patients without prior AF.

Table 4. Atrial Fibrillation–Related Health Utilization After Cardiac Surgery in Propensity Score–Matched Patients

	No LAAO				LAAO						
Outcome	No. of Patients	No. of Events	Person-Years	Event Rate[a]	No. of Patients	No. of Events	Person-Years	Event Rate[a]	Absolute Rate Difference (95% CI)[a]	Incident Rate Ratio (95% CI)	*P* Value
AF-Related Outpatient Visits											
Overall	4295	79 951	7792	10.26	4295	96 676	8083	11.96	1.70 (1.60-1.80)	1.17 (1.10-1.24)	<.001
AF at baseline	3219	75 825	5782	13.11	3219	90 927	6171	14.74	1.62 (1.49-1.76)	1.12 (1.06-1.19)	<.001
No AF at baseline	1076	4126	2010	2.05	1076	5749	1912	3.01	0.95 (0.85-1.05)	1.46 (1.10-1.96)	.01
AF-Related Hospitalization											
Overall	4295	2473	7792	0.32	4295	2891	8083	0.36	0.04 (0.02-0.06)	1.13 (1.05-1.21)	.002
AF at baseline	3219	2360	5782	0.41	3219	2738	6171	0.44	0.04 (0.01-0.06)	1.09 (1.01-1.17)	.03
No AF at baseline	1076	113	2010	0.06	1076	153	1912	0.08	0.02 (0.01-0.04)	1.42 (1.01-2.00)	.04

Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage.

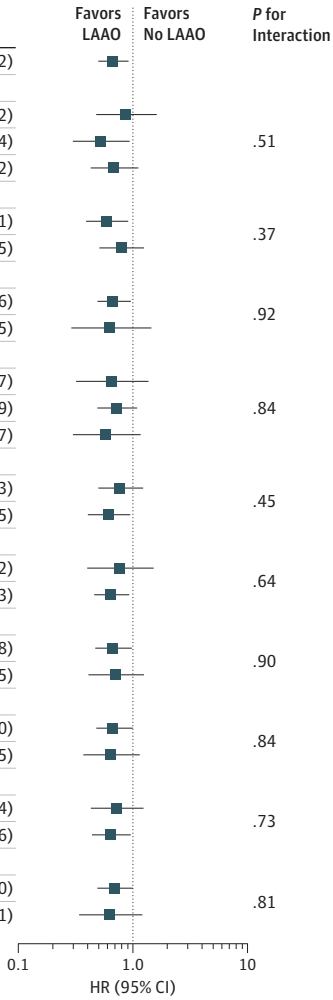
[a] Calculated as the number of events per person-year.

0.02 [95% CI, 0.01 to 0.04] event per person-year; rate ratio, 1.42 [95% CI, 1.01 to 2.00]; *P* = .04) for hospitalizations (Table 4).

In the multivariable regression using data from all 50 061 patients without prior AF, LAAO was associated with an increased risk of postoperative AF (HR, 1.48 [95% CI, 1.31 to 1.67]; *P* < .001). Other variables associated with postoperative AF included older age, a valve procedure, and a history of other supraventricular arrhythmia (eTable 3 in Supplement 2).

Figure 2. Subgroup Analysis for Stroke in Propensity-Matched Patients With Atrial Fibrillation at Baseline

Subgroup	No LAAO				LAAO				HR (95% CI)	P for Interaction
	No. of Patients	No. of Events	Person-Years	Event Rate per 100 Person-Years	No. of Patients	No. of Events	Person-Years	Event Rate per 100 Person-Years		
All patients	3219	97	5683	1.71	3219	67	6032	1.11	0.68 (0.50-0.92)	
Age, y										
18-64	892	22	1542	1.43	923	20	1626	1.23	0.88 (0.48-1.62)	
65-74	1138	33	1929	1.71	1168	19	2194	0.87	0.53 (0.30-0.94)	.51
≥75	1189	42	2212	1.90	1128	28	2212	1.27	0.70 (0.43-1.12)	
Sex										
Men	2062	55	3538	1.55	2092	34	3826	0.89	0.59 (0.39-0.91)	.37
Women	1157	42	2144	1.96	1127	33	2206	1.50	0.80 (0.51-1.25)	
Race										
White	2605	83	4778	1.74	2582	57	4985	1.14	0.68 (0.49-0.96)	.92
Nonwhite	614	14	904	1.55	637	NA[a]	NA[a]	0.95	0.64 (0.29-1.45)	
Surgery types										
Isolated CABG	807	17	1359	1.25	894	13	1576	0.83	0.67 (0.32-1.37)	
Valve replacement	1544	58	2751	2.11	1494	41	2744	1.49	0.73 (0.49-1.09)	.84
Valve repair	868	22	1573	1.40	831	13	1712	0.76	0.59 (0.30-1.17)	
CHA2DS2-VASc score[b]										
<4	1922	41	3444	1.19	1994	34	3760	0.90	0.78 (0.50-1.23)	.45
≥4	1297	56	2239	2.50	1225	33	2272	1.45	0.62 (0.40-0.95)	
HAS-BLED score[c]										
<3	997	19	1838	1.03	1074	16	2007	0.80	0.78 (0.40-1.52)	.64
≥3	2222	78	3845	2.03	2145	51	4024	1.27	0.65 (0.46-0.93)	
Prior thromboembolism										
No	2551	66	4555	1.45	2606	47	4976	0.94	0.68 (0.47-0.98)	.90
Yes	668	31	1127	2.75	613	20	1056	1.89	0.71 (0.41-1.25)	
Prior bleeding										
No	2358	67	4247	1.58	2408	48	4555	1.05	0.69 (0.48-1.00)	.84
Yes	861	30	1436	2.09	811	19	1477	1.29	0.65 (0.37-1.15)	
History of heart failure										
No	1276	31	2356	1.32	1321	24	2534	0.95	0.73 (0.43-1.24)	.73
Yes	1943	66	3326	1.98	1898	43	3498	1.23	0.65 (0.44-0.96)	
History of stage 3-5 CKD										
No	2727	72	4946	1.46	2763	52	5286	0.98	0.70 (0.49-1.00)	.81
Yes	492	25	737	3.39	456	15	745	2.01	0.64 (0.34-1.21)	



AF indicates atrial fibrillation; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LAAO, surgical occlusion of the left atrial appendage; NA, not available.

[a] To maintain deidentification, OptumLabs does not allow researchers to disclose the number of events when the number is 10 or fewer. Medicare data have similar requirements.

[b] The CHA_2DS_2-VASc score is a 0- to 9-point stroke risk score for which a higher point score indicates higher risk of stroke. The point score is calculated as follows: 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex; 2 points for age 75 years or older and prior stroke, transient ischemic attack, or thromboembolism.

[c] The HAS-BLED score is a 0- to 9-point bleeding risk score for which a higher point score indicates higher risk of bleeding. The point score is calculated as follows: 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio, older than 65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider international normalized ratio, so the range is 0-8.

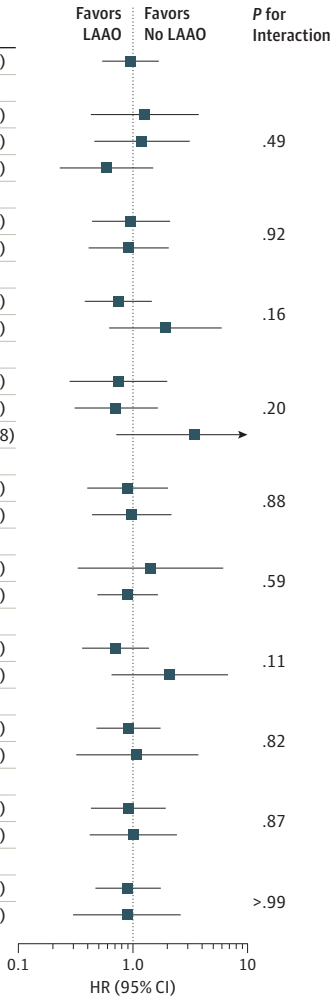
Sensitivity Analyses

The subgroup analyses were consistent with the main findings (**Figure 2** and **Figure 3**; eFigures 1 and 2 in Supplement 2). For example, *P* values for interaction were nonsignificant for age, sex, CHA_2DS_2-VASc score, and chronic kidney disease. There were no significant relationships between LAAO and any of the falsification end points (HR, 0.94 [95% CI, 0.73 to 1.20]; *P* = .60 for chronic obstructive pulmonary disease; HR, 0.92 [95% CI, 0.81 to 1.05]; *P* = .20 for pneumonia; and HR, 0.91 [95% CI, 0.75 to 1.11]; *P* = .34 for fracture) in the overall cohort (eTable 4 in Supplement 2). The results using the propensity score weighting method were also consistent with the main findings (HR, 0.76 [95% CI, 0.61 to 0.95]; *P* = .02 for stroke and HR, 0.78 [95% CI, 0.68 to 0.90]; *P* < .001 for mortality in the overall cohort) (eTables 5 and 6 in Supplement 2).

The use of oral anticoagulants over time was similar between patients undergoing and not undergoing LAAO in the propensity score–matched cohort (eFigure 3 in Supplement 2), which suggested that the associations seen with LAAO were not related to differential use of oral anticoagulants. The associations between LAAO and stroke or mortality stratified by oral anticoagulant use during follow-up was consistent with the main findings,

Figure 3. Subgroup Analysis for Stroke in Propensity-Matched Patients Without Atrial Fibrillation at Baseline

Subgroup	No LAAO				LAAO				HR (95% CI)	P for Interaction
	No. of Patients	No. of Events	Person-Years	Event Rate per 100 Person-Years	No. of Patients	No. of Events	Person-Years	Event Rate per 100 Person-Years		
All patients	1076	25	1982	1.26	1076	23	1877	1.23	0.95 (0.54-1.68)	
Age, y										
18-64	539	NA[a]	NA[a]	0.60	519	NA[a]	NA[a]	0.76	1.27 (0.43-3.75)	
65-74	323	NA[a]	NA[a]	1.35	329	NA[a]	NA[a]	1.68	1.20 (0.46-3.13)	.49
≥75	214	11	384	2.87	228	NA[a]	NA[a]	1.68	0.59 (0.23-1.50)	
Sex										
Men	718	13	1324	0.98	697	12	1232	0.97	0.96 (0.44-2.11)	
Women	358	12	658	1.82	379	11	644	1.71	0.92 (0.41-2.05)	.92
Race										
White	819	20	1553	1.29	839	15	1567	0.96	0.75 (0.38-1.46)	
Nonwhite	257	NA[a]	NA[a]	1.17	237	NA[a]	NA[a]	2.58	1.92 (0.62-5.94)	.16
Surgery types										
Isolated CABG	366	NA[a]	NA[a]	1.58	361	NA[a]	NA[a]	1.30	0.75 (0.28-1.99)	
Valve replacement	395	13	712	1.83	385	NA[a]	NA[a]	1.27	0.71 (0.31-1.65)	.20
Valve repair	315	NA[a]	NA[a]	0.31	330	NA[a]	NA[a]	1.11	3.43 (0.71-16.58)	
CHA2DS2-VASc score[b]										
<4	812	13	1552	0.84	803	11	1431	0.77	0.90 (0.40-2.02)	
≥4	264	12	430	2.79	273	12	445	2.69	0.98 (0.44-2.17)	.88
HAS-BLED score[c]										
<3	490	NA[a]	NA[a]	0.31	488	NA[a]	NA[a]	0.44	1.42 (0.33-6.13)	
≥3	586	22	1029	2.14	588	19	962	1.97	0.89 (0.49-1.65)	.59
Prior thromboembolism										
No	938	21	1757	1.20	921	14	1640	0.85	0.70 (0.36-1.38)	
Yes	138	NA[a]	NA[a]	1.77	155	NA[a]	NA[a]	3.81	2.09 (0.65-6.75)	.11
Prior bleeding										
No	885	20	1645	1.22	842	17	1529	1.11	0.91 (0.48-1.74)	
Yes	191	NA[a]	NA[a]	1.48	234	NA[a]	NA[a]	1.73	1.08 (0.32-3.72)	.82
History of heart failure										
No	617	15	1217	1.23	607	13	1096	1.19	0.91 (0.43-1.93)	
Yes	459	NA[a]	NA[a]	1.31	469	NA[a]	NA[a]	1.28	1.01 (0.42-2.42)	.87
History of stage 3-5 CKD										
No	965	19	1818	1.05	937	16	1647	0.97	0.90 (0.47-1.75)	
Yes	111	NA[a]	NA[a]	3.65	139	NA[a]	NA[a]	3.05	0.89 (0.30-2.61)	>.99



AF indicates atrial fibrillation; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LAAO, surgical occlusion of the left atrial appendage; NA, not available.

[a] To maintain deidentification, OptumLabs does not allow researchers to disclose the number of events when the number is 10 or fewer. Medicare data have similar requirements.

[b] The CHA_2DS_2-VASc score is a 0- to 9-point stroke risk score for which a higher point score indicates higher risk of stroke. The point score is calculated as follows: 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex; 2 points for age 75 years or older and prior stroke, transient ischemic attack, or thromboembolism.

[c] The HAS-BLED score is a 0- to 9-point bleeding risk score for which a higher point score indicates higher risk of bleeding. The point score is calculated as follows: 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio, older than 65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider international normalized ratio, so the range is 0-8.

except that the association between LAAO and stroke was not significant among patients with AF taking oral anticoagulation (HR, 0.80 [95% CI, 0.51 to 1.24]) (eTable 7 in Supplement 2).

Long-term AF-related health utilization excluding the first 30 days was higher for patients who had postoperative AF than for those who did not (6.68 vs 0.61 outpatient visits per person-year; absolute difference, 6.07 [95% CI, 5.89 to 6.24] event per person-year; $P < .001$ and 0.14 vs 0.02 hospitalization per person-year; absolute difference, 0.12 [95% CI, 0.10 to 0.15] event per person-year; $P < .001$), suggesting that patients with postoperative AF were at a higher risk of developing late AF (eTable 8 in Supplement 2).

In patients who did not have prior AF but developed AF during follow-up, LAAO was not associated with a significant reduction in stroke (HR, 0.74 [95% CI, 0.34 to 1.62]) or mortality (HR, 0.73 [95% CI, 0.41 to 1.30]) (eTable 9 in Supplement 2). The majority of the patients (1430/2152 [66.4%]) without prior AF at the time of the surgery did not develop AF during follow-up. Adjusting for concomitant Maze procedure did not substantially affect the results (eTable 10 in Supplement 2).

Discussion

In this large heterogeneous cohort of patients undergoing cardiac surgery, concurrent LAAO was associated with reduced risk of stroke and all-cause mortality and was associated with increased AF-related health care utilization.

This study is the first to our knowledge to investigate associations between LAAO and clinical outcomes stratified by preexisting AF.[20] The interaction between LAAO and prior AF was not statistically significant, which did not support a difference in the relative risk reduction with LAAO between patients with and without prior AF. In the current study, 1 in 4 patients undergoing LAAO did not have documented preoperative AF, and the absolute risk reduction for stroke and mortality associated with LAAO was small in these patients. However, the confidence intervals were wide, and thus, future studies with larger sample sizes will be needed to fully assess the interaction and the role of LAAO in patients without prior AF. The consideration of preemptive LAAO in patients without documented preoperative AF must be balanced against the fact that the majority of patients would not develop AF after the surgery and LAAO may be associated with an increased risk of subsequent AF.

One in 3 patients in this cohort undergoing cardiac surgery had a history of AF, which is related to increased risks of stroke and mortality,[2,3,21] and lifelong use of oral anticoagulants is recommended in 80% to 90% of patients with AF to prevent stroke.[22,23] However, fewer than half of the patients with AF in practice adhere to oral anticoagulation,[24] and 1 in 6 patients is deemed unsuitable for oral anticoagulation by his or her physician.[25] Furthermore, some patients are still at a high risk of stroke despite oral anticoagulation treatment.[26] Therefore, LAAO may be an option for patients with AF who have difficulty taking oral anticoagulant drugs and for those who desire further risk reduction in addition to anticoagulation. In our study, the association between LAAO and stroke was not significant among patients with AF who were taking oral anticoagulation. This could be attributable to the small number of events and patients in the subgroup, as well as the possibility that oral anticoagulation already reduced the risk of stroke, and the additional risk reduction from LAAO was relatively smaller than that seen in patients who did not receive oral anticoagulation.

In patients with prior AF and in those without prior AF, LAAO was associated with a higher rate of AF-related health utilization during follow-up, which supports the previous observation that LAAO may be associated with subsequent AF.[6] Although this study cannot directly measure the frequency and length of AF episodes, the increased number of AF-related outpatient visits and hospitalizations provided an important measure of the AF-related burden to patients and the health care system. Recent studies suggested that patients who developed postoperative AF incur a mean of $10 000 to $20 000 in additional hospital treatment costs, 12 to 24 hours of additional intensive care unit time, and an additional 2 to 5 days in the hospital.[27] As such, the risk of subsequent AF needs to be discussed with patients during shared decision making.

The current study may have greater generalizability than previous studies, because it included a large number of patients of all ages and races undergoing cardiac surgery at a diverse range of institutions across the United States. The findings in patients with AF were consistent with those from a recent observational study,[5] but that previous study was limited to patients 65 years and older who had prior AF, which represented only about 24% of all patients undergoing cardiac surgery in the current study. A randomized trial of 187 patients also found a lower risk of stroke with LAAO but did not find a difference in mortality, perhaps because of the small sample size.[28] The ongoing Left Atrial Appendage Occlusion Study III trial (NCT01561651) plans to enroll 4700 patients, but that trial was limited to high-risk patients with documented AF or atrial flutter undergoing CABG and will not address the population without AF or those undergoing valve surgery.

Limitations

This study has several limitations. First, despite statistical adjustment, the study may still be subject to confounding. Some of the variables measured, eg, prior treatment with ablation, cardioversion, antiarrhythmic drugs, and medications for other chronic conditions, could be proxies for unmeasured aspects of the underlying diseases. Furthermore, the test of falsification end points provided some reassurance that there was no evidence for residual confounding.

Second, the study relied on administrative data to ascertain baseline characteristics and outcomes, which could be subject to misclassification. For example, the postoperative AF may have been undercoded, but in patients without prior AF, 24% had postoperative AF, which was consistent with previous reports.[29] Furthermore, it was unlikely there was any systemic difference in the ascertainment of comorbidities and outcomes between the 2 treatment groups, and thus, the misclassification should not have meaningfully affected the comparisons. The diagnosis and procedure codes used in this study were commonly used in previous studies and demonstrated good performance in validation studies, with positive predictive values around 90%.[30-37]

Third, this study was unable to distinguish between LAAO by excision or by exclusion using sutures or stapling, because these procedures are all described by a single code. Nor were data available on the apparent success of closure as gauged by intraoperative transesophageal echocardiography.

Fourth, the number of patients without prior AF undergoing LAAO was relatively small and the confidence intervals around the point estimates were relatively wide. However, since the absolute reduction in stroke risk was only 0.04 event per 100 person-years in this group, it would require an extremely large sample to detect such a small, and potentially clinically insignificant, difference.

Conclusions

Among patients undergoing cardiac surgery, concurrent surgical LAAO, compared with no surgical LAAO, was associated with reduced risk of subsequent stroke and all-cause mortality. Further research, including from randomized clinical trials, is needed to more definitively determine the role of surgical LAAO.

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