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Is Anticoagulation Warranted after Left Atrial Appendage Ligation in Patients at Risk for Stroke after Cardiac Surgery?

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Abstract

Objectives: Left atrial appendage ligation (LAAL) may constitute alternative stroke prophylaxis in patients with atrial fibrillation (AF). Herein we describe the 30-day post discharge outcomes of cardiac surgery patients with elevated stroke risk with or without anticoagulation (AC) following epicardial LAAL. **Methods:** Data were reviewed for 479 consecutive adult patients who underwent epicardial LAAL from 2014-2019 (median CHA_2DS_2-VASc score = 4.0). There were 251 and 228 patients discharged with and without AC, respectively, who were followed for 30 days. Patients were matched via 1:1 Propensity Score Matching (PSM; n = 115 per group). Post-discharge outcomes included stroke, bleeding, readmission for cardiac re-intervention, mortality, and a composite endpoint comprised of the aforementioned outcomes. **Results:** There was no difference in post-discharge stroke incidence regardless of AC (adjusted cumulative incidence (ACI) 0.009 CI [0.001 - 0.043] with AC vs 0.009 CI [0.001 - 0.43] without AC; p = 0.826), post-discharge bleeding (ACI 0.018 CI [0.003 - 0.057] with AC vs 0.009 CI [0.001 - 0.046] without AC; p = 0.738), readmission for cardiac re-intervention (ACI 0.009 CI [0.009 - 0.009] with AC vs 0 CI [NA] without AC; p = 0.340, post-discharge mortality (ACI 0 CI NA with AC vs 0.009 CI [0.001 - 0.046] without AC; p = 0.123, or in the composite outcome (ACI 0.026 CI [0.007 - 0.069] with AC vs 0.027 CI [0.007 - 0.071] without AC; p = 0.824. **Conclusion:** Cessation of AC in patients with elevated stroke risk following epicardial LAAL during cardiac

surgery does not affect stroke rate, mortality, or bleeding incidence up to 30 days post-discharge in this preliminary analysis.

Keywords

Arrhythmias, Minimally Invasive Surgery, Perioperative Care

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide [1]. New-onset postoperative AF (POAF) occurs in up to 42% of cardiac and 10% of non-cardiac surgery patients [2]. AF increases the risk of stroke to 4 - 5 times that of a patient without AF [3] [4] and accounts for at least one-third of all ischemic strokes [5]. Although contested, the left atrial appendage (LAA) putatively serves as the nidus for thrombus formation in up to 90% of patients with non-valvular AF [6] [7]. Anticoagulation (AC) with either vitamin K antagonists or direct oral anticoagulants (DOACs) remains the gold standard for thromboembolism prophylaxis in AF patients; however, LAA ligation (LAAL) has emerged as a promising therapy to reduce stroke risk, particularly in those at risk for bleeding or with other contraindications to therapeutic anticoagulation. Nevertheless, there remains a paucity of prospective clinical data directly evaluating the role of AC following LAAL in patients with non-valvular AF or without AF [2] [8] [9]. Herein we report our experience with AC in patients with elevated risk of stroke following epicardial LAAL after cardiac surgery in patients both with and without AF, with the hypothesis that LAAL can provide sufficient stroke risk reduction from preexisting or POAF in the early postoperative period in which bleeding risk is elevated.

2. Patients and Methods

2.1. Patients

The inclusion criteria were all patients who underwent open cardiac surgery with concomitant LAAL (AtriClip, AtriCure, Mason, OH) at a single institution between March 2014 and October 2019 were identified. Eligibility for LAAL was determined by individual surgeon preference and patient consent—LAAL was offered on a case-by-case basis and, in general, patients who were at elevated risk for postoperative complications from early initiation of AC and/or with an elevated risk of stroke according to CHA_2DS_2-VASc score (score greater than or equal to 3 in general) were offered LAAL. The exclusion criteria were patients < 18 years old, undergoing congenital heart surgery, those with mitral stenosis or with perioperative shock or endocarditis were excluded. All patients were reviewed and/or contacted via phone to obtain routine follow-up data, with chart-based follow-up information limited to subsequent encounters at either our institution or an affiliated institution with accessible data. Follow up was 100% for

the matched and unmatched cohorts at 30 days. Complete LAA exclusion was confirmed at the end of each case with transesophageal echocardiography (TEE). Patients who received postoperative AC (warfarin, apixaban, rivaroxaban, or dabigatran) with continuation past hospital discharge were marked as "AC," whereas those who did not receive AC postoperatively were labeled as "no AC." The decision to initiate, continue, or discontinue prophylactic AC therapy at time of hospital discharge was made on a case-by-case basis by a multidisciplinary heart team, factoring in such patient characteristics as risk of stroke, persistent atrial fibrillation, risk of bleeding, predicted patient compliance, age, and patient preference.

2.2. Study Endpoints

Clinical data was obtained through a combination of chart review and follow-up phone calls. The primary endpoint was post-discharge stroke, and secondary outcomes included post-discharge bleeding, readmission for cardiac re-intervention, mortality, and a composite outcome comprised of post-discharge stroke, post-discharge bleeding, readmission for cardiac re-intervention, and mortality. Stroke diagnosis was adjudicated by neurology consult notes describing clinical suspicion of stroke with concordant radiologic findings.

2.3. Data Definitions

Data definitions, unless otherwise specified, are compliant with those of the New York State Department of Health (NYSDOH) Cardiac Surgery data collection form (https://www.health.ny.gov/forms/cardiac_surgery/). Change and collation in definitions and where they occurred are included in **Supplemental Appendix 1**. Hypertension (HTN) and preoperative AF diagnoses were identified from pre-existing International Classification of Diseases (ICD) 9th and 10th edition codes, whereas POAF was identified by postoperative electrocardiogram. Missing data is outlined in **Supplemental Table S1**. No variable was missing ≥ 2%. All missing preoperative data was imputed via random forest based on other preoperative data. Procedure categories are grouped as outlined in **Supplemental Table S2**.

2.4. Statistical Analysis

The "car," "mice," "MatchIt," "cmprsk," and "tableone," packages of R statistical software [10] were used for statistical analysis and all data figures. Data are expressed as frequencies and percentages for categorical variables. Continuous variables are expressed as either mean (SD) or median (IQR) depending on normality which was tested via QQ Plots, and were compared using the t-test or Mann-Whitney test, respectively. Categorical variables were compared using Chi-Square or Fisher's exact test depending on size (>5). Logistic regression was performed with AC as the dependent variable and all preoperative risk variables in **Table 1** as independent variables in order to generate scores of propensity to

Table 1. Preop Characteristics pre- and post-propensity score matched patients.

Patient Characteristics	Unadj. AC (n = 251)	Unadj. No AC (n = 228)	SMD	Adj. AC (n = 116)	Adj. No AC (n = 116)	SMD
Age, median [IQR]	71.0 [64.0 - 76.0]	69.5 [63.0 - 76.0]	0.075	71.0 [63.0 - 77.0]	70.0 [61.8 - 77.0]	0.006
Female, n (%)	94 (37.5)	82 (36.0)	0.031	43 (37.1)	35 (30.2)	0.146
BMI, median [IQR]	27.3 [24.4 - 31.4]	28.1 [25.0 - 31.9]	0.022	27.3 [24.0 - 30.9]	27.7 [25.0 - 31.1]	0.008
Hispanic Ethnicity, n (%)	32 (12.7)	36 (15.8)	0.087	18 (15.5)	20 (17.2)	0.047
PreopAfib, n (%)	179 (71.3)	48 (21.1)	1.167	50 (43.1)	45 (38.8)	0.088
Procedure, n (%)			0.363			0.357
Aorta	28 (11.2)	48 (21.1)		12 (10.3)	22 (19.0)	
Total Valve	133 (53.0)	85 (37.3)		58 (50.0)	50 (43.1)	
Total CABG	47 (18.7)	54 (23.7)		18 (15.5)	26 (22.4)	
Total Valve/CABG	43 (17.1)	41 (18.0)		28 (24.1)	18 (15.5)	
Elective Procedure, n (%)	151 (60.2)	139 (61.0)	0.016	71 (61.2)	69 (59.5)	0.035
Diabetes, n (%)	60 (23.9)	76 (33.3)	0.210	31 (26.7)	37 (31.9)	0.114
Renal Failure, n (%)	2 (0.8)	5 (2.2)	0.115	0 (0)	0 (0)	<0.001
CVD, n (%)	48 (19.1)	44 (19.3)	0.004	23 (19.8)	22 (19.0)	0.022
CLD, n (%)	46 (18.3)	27 (11.8)	0.182	23 (19.8)	18 (15.5)	0.113
PVD, n (%)	35 (13.9)	50 (21.9)	0.209	21 (18.1)	25 (21.6)	0.087
CHF, n (%)	137 (54.6)	86 (37.7)	0.343	58 (50.0)	52 (44.8)	0.104
Previous Organ Tx, n (%)	3 (1.2)	3 (1.3)	0.011	0 (0)	0 (0)	<0.001
Previous MI, n (%)	197 (78.5)	182 (79.8)	0.033	90 (77.6)	95 (81.9)	0.107
Previous Surgery, n (%)	22 (8.8)	8 (3.5)	0.220	11 (9.5)	6 (5.2)	0.166
Creatinine, median [IQR]	1.1 [0.9 - 1.3]	1.0 [0.9 - 1.2]	0.037	1.0 [0.9 - 1.2]	1.0 [0.9 - 1.3]	0.106
CHA_2DS_2-VASc Score	4.0 [3.0 - 5.0]	4.0 [3.0 - 6.0]	0.073	4.0 [3.0 - 5.0]	4.0 [3.0 - 6.0]	0.048
Prior/Concomitant Ablation, n (%)	136 (54.2)	40 (17.5)	0.827	42 (36.2)	37 (31.9)	0.091
EF, median [IQR]	55.0 [49.0 - 63.0]	58.0 [51.0 - 63.0]	0.097	55.5 [49.8 - 63.0]	58.0 [53.0 - 63.0]	0.009
HTN, n (%)	205 (81.7)	191 (83.8)	0.056	92 (79.3)	90 (77.6)	0.042
New Onset POAF, n (%)	201 (82.4)	96 (43.8)	0.871	83 (71.6)	86 (74.1)	0.058

AC = anticoagulation; Adj. = Adjusted; BMI = body mass index; BP = blood pressure; BSA = body surface area; CABG = coronary artery bypass graft; CHF = congestive heart failure; CLD = chronic lung disease; CVD = cerebrovascular disease; EF = ejection fraction; HTN = hypertension; Preop = preoperative; POAF = postoperative atrial fibrillation; PVD = peripheral vascular disease; SMD = standardized mean difference; Sx = symptoms; Unadj. = Unadjusted.

receive or not receive AC. Variables in the model were checked for collinearity using the Variance Inflation Factor (VIF). The CHA_2DS_2-VASc score was found to be collinear (VIF > 10) and was removed from the model.

Propensity score matching (PSM) was utilized, whereby patients were matched at a 1:1 ratio for AC:no AC and a 0.2 caliper was used. The caliper is the number

of standard deviations of logit of the propensity score and used as a cut-off point in determining matches. Matching success was determined via standardized mean difference (SMD) < 0.1 on variables post-match. Matched groups were compared in a variety of ways. Because post-discharge stroke, readmission, and re-intervention have death as a competing event, the two groups' cumulative incidence functions were compared using Fine and Gray's method [11]. Mortality was analyzed by the method of Kaplan and Meier and was compared via the log rank test. Because of the sample size and few events, confidence intervals were calculated using a log (-log) transformation [12]. Bonferroni correction was used to protect against inflated Type 1 error (p-value of 0.01 = significant).

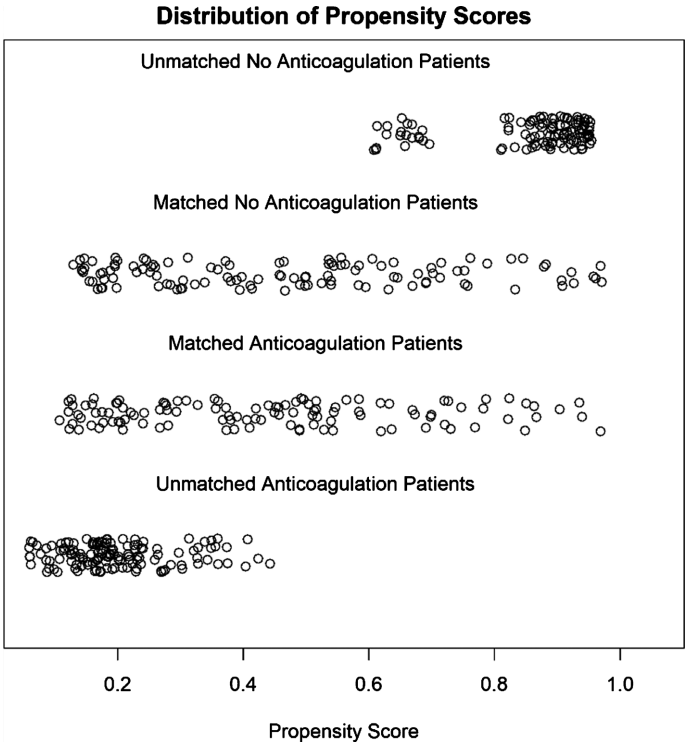
2.5. Ethical Statement

This protocol (#AAAK3154, approved 7/10/2020) was approved by the Columbia University Irving Medical Center Institutional Review Board with waiver of patient consent.

3. Results

Of the 479 total patients (medianCHA_2DS_2-VASc score = 4.0), 251 were discharged with postoperative AC, whereas 228 did not receive AC. In the unadjusted analyses, there were marked differences in preoperative risk factors between groups (**Table 1**). The AC group was characterized by a higher incidence of preoperative AF, chronic lung disease (CLD), congestive heart failure (CHF), prior surgery, and prior/concomitant ablation procedures. The no AC group had a higher incidence of diabetes mellitus (DM), renal failure, peripheral vascular disease (PVD), and new-onset POAF. After PSM, the two groups of 115 patients each were well-matched (**Figure 1**). Only procedure type and prior/concomitant ablation had an SMD > 0.1, though ablation was the difference of one patient. Although the CHA_2DS_2-VASc score could not be factored into the PSM, it did have an SMD < 0.1 post-match. In the adjusted analysis there was no difference in post-discharge stroke incidence regardless of AC (adjusted cumulative incidence (ACI) 0.009 CI [0.001 - 0.043] with AC vs 0.009 CI [0.001 - 0.43] without AC; p = 0.826), post-discharge bleeding (ACI 0.018 CI [0.003 - 0.057] with AC vs 0.009 CI [0.001 - 0.046] without AC; p = 0.738), readmission for cardiac re-intervention (ACI 0.009 CI [0.009 - 0.009] with AC vs 0 CI [NA] without AC; p = 0.340, post-discharge mortality (ACI 0 CI NA with AC vs 0.009 CI [0.001 - 0.046] without AC; p = 0.123, or in the composite outcome (ACI 0.026 CI [0.007 - 0.069] with AC vs 0.027 CI [0.007 - 0.071] without AC; p = 0.824 (**Table 2**, **Figure 2**). All strokes (n = 5 on AC, n = 5 without AC) were ischemic in etiology, with one patient in the "no AC" group demonstrating hemorrhagic conversion.

We performed a similar analysis at one year which also showed that there was no difference in post-discharge stroke incidence regardless of AC (adjusted cumulative incidence (ACI) 0.035 CI [0.009 - 0.093] with AC vs 0.067 CI [0.024 -



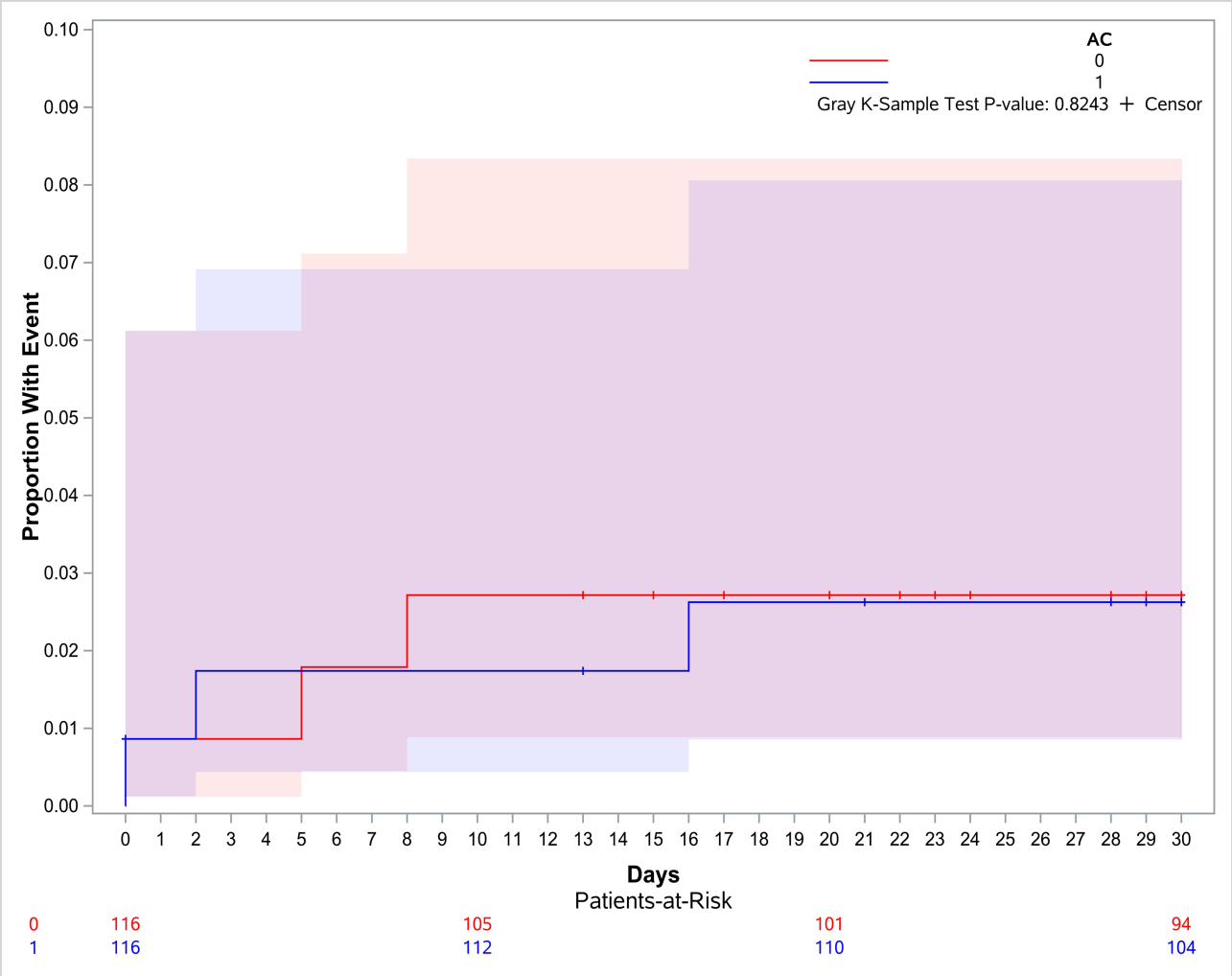
Legend: Distribution of propensity scores after matching.

Figure 1. Distribution of propensity scores.

Table 2. Outcomes for the matched study cohort.

	Number of 30-day Outcomes	Number of Competing Events (death) prior to outcome	Cumulative Incidence at 30 days	CI	P-value
Stroke*					0.826
Anticoagulant	5	0	0.009	[0.001 - 0.043]	
No Anticoagulant	5	2	0.009	[0.001 - 0.043]	
Postoperative Bleeding*					0.738
Anticoagulant	3	0	0.018	[0.003 - 0.057]	
No Anticoagulant	2	1	0.009	[0.001 - 0.046]	
Readmission for Cardiac Re-Intervention*					0.34
Anticoagulant	1	0	0.009	[0.009 - 0.009]	
No Anticoagulant	0	2	0	[NA]	
Mortality					0.123
Anticoagulant	0	NA	0	[NA]	
No Anticoagulant	2	NA	0.009	[0.001 - 0.046]	
Composite Outcome					0.824
Anticoagulant	8	NA	0.026	[0.007 - 0.069]	
No Anticoagulant	8	NA	0.027	[0.007 - 0.071]	

*Used Fine and Gray competing risk.



Legend: cumulative 30-day incidence of the composite endpoint in patients who underwent left atrial appendage ligation and were discharged with or without anticoagulation.

Figure 2. Cumulative incidence of the composite outcome.

0.141] without AC; p = 0.400), post-discharge bleeding (ACI 0.027 CI [0.007 - 0.070] with AC vs 0.028 CI [0.005 - 0.093] without AC; p = 0.727), readmission for cardiac re-intervention (ACI 0.013 CI [0.001 - 0.062] with AC vs 0 CI [NA] without AC; p = 0.348, post-discharge mortality (ACI 0.013 CI [0.001 - 0.062] with AC vs 0.023 CI [0.004 - 0.075] without AC; p = 0.495, or in the composite outcome (ACI 0.088 CI [0.041 - 0.159] with AC vs 0.118 CI [0.056 - 0.206] without AC; p = 0.655 (**Supplemental** Table S3 and **Supplemental** Figure S1). Though these results suffered from poor follow-up--follow-up after discharge for the matched cohort up to 1 year was 44.78% for stroke, 47.39% for mortality, and 43.04% for the composite outcome—comparison between the follow up and no follow up groups showed they were very similar for each outcome, with the group that followed up actually having slightly higher rates of preoperative atrial fibrillation, chronic lung disease, and diabetes in two of the outcomes (**Supplemental** Tables S4-S6).

4. Discussion

The age-adjusted incidence of AF in the US is expected to increase to 12.1 million patients by 2030 [13], which may be further augmented by continued discussions about the utility of AF screening and the increasing availability of smartwatches with electrocardiogram (ECG)-monitoring capabilities [14] [15] [16]. In patients with AF and a CHA_2DS_2-VASc score ≥ 2 if male or ≥3 in female without contraindications, AC with either warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban is indicated for stroke prophylaxis [17]. Clinical trials have demonstrated bleeding rates up to 0.4% - 3.0% (after 1 year) and 0.1% - 0.9% (after 12 - 15 months) associated with chronic vitamin K antagonists and DOACs use, respectively [18]. Our results suggest that the absence of post-discharge therapeutic anticoagulation does not impact the 30 day incidences of stroke, mortality, or major bleeding in patients with an elevated CHA_2DS_2-VASc score who undergo epicardial LAAL during cardiac surgery. Thus the risk and benefits of pharmacologic stroke prophylaxis versus early postoperative bleeding risk in these patients must be considered carefully when effective LAAL exclusion has been acheived [18] [19] [20].

A multitude of percutaneous and surgical techniques and devices have been implemented for LAA exclusion in patients with AF, particularly in those with recalcitrant arrythmogenicity or for whom AC is contraindicated [21] [22] [23]. Percutaneous LAA closure devices for stroke prevention in patients with non-valvular AF is an effective, minimally-invasive strategy, particularly if contraindications to AC and surgical intervention are present [24] [25] [26], Surgicalexclusion of the LAA, whether by resection or by suture excision or staple-ligation, remains a viable albeit invasive method of LAAL, which can be performed in patients with additional indications for open cardiothoracic surgery or as an isolated procedure. Furthermore, the LAOS III trial showed that among participants with atrial fibrillation who had undergone cardiac surgery, most of whom continued to receive ongoing antithrombotic therapy, the risk of ischemic stroke or systemic embolism was lower with concomitant left atrial appendage occlusion performed during the surgery than without it. Concomitant surgical LAAL does not appear to contribute to any increase in postoperative complications compared to outcomes of the concomitant surgical procedure alone, and has demonstrated reduced incidences of postoperative stroke and all-cause mortality in retrospective analyses [27] [28]. Although an increased incidence of new-onset POAF has been suggested in patients following LAAL [29]. In contrast, percutaneous techniques as standalone procedures incur a higher rate of complications than surgical concomitant LAAL and may complicate the risk-benefit relationship of prophylactic LAAL. Complications of percutaneous access include bleeding, fistulae, hematomas, or pseudoaneurysms, and transseptal left atrial access has been associated with air embolisms, stroke, iatrogenic perforation, and pericardial effusions resulting in cardiac tamponade [30] [31]. Whether the approach is surgical or percutaneous, incomplete closure of the LAA following LAAL is

associated with a significantly increased risk of post-procedural stroke in a manner inversely proportional to the size of the LAAL defect [32].

Per 2019 American Heart Association and American College of Cardiology guidelines, surgical LAAL may be considered in patients with AF undergoing cardiac surgery (Class of Recommendation: IIb; Level of Evidence B-NR), whereas percutaneous LAAL may be considered for patients with AF at an elevated risk for thromboembolism and a contraindication for AC therapy [17]. However, the role of prophylactic LAAL in patients without AF is poorly defined. Given the high incidence of POAF in cardiac surgery patients, epicardial LAAL during cardiac surgery in patients without AF offers a mechanism by which surgeons can potentially obviate the need for AC in patients who go on to develop persistent AF or suffer complications related to AC early after surgery. For this reason, LAAL for patients with an elevated CHA_2DS_2-VASc score who are at risk for bleeding complications may be reasonable candidates for concomitant surgical LAAL. Furthermore, prophylactic LAAL during cardiac surgery may confer a decreased risk of stroke for patients regardless of the presence of absence of AF [28]. Thus, even in patients without high-risk features, prophylactic LAAL during cardiac surgery is a low-risk procedure that may circumvent the need for AC in patients who develop new-onset POAF, pending further prospective investigation. In our study, we demonstrate that early stroke rates were overall equivalent and low in patients that underwent LAAL with or without AC, which is unsurprising. Moreover, although bleeding events were also similar in this small series, it can be expected that postoperative bleeding may be increased within 30 days if AC is initiated early after surgery. Protection from stroke in this period from thromboemboli originating from the left atrium may be conferred by LAAL, and allow for later resumption (or no resumption at all) of AC once the risk of surgical bleeding has been sufficiently reduced (*i.e.*, in an outpatient setting). Factors that may affect this decision include left atrial ablation and ablation type (cryo versus radiofrequency), other indications for AC such as deep venous thromboses, pulmonary embolism, obesity or mechanical heart valves, or the need for multiple anticoagulants (such as warfarin plus dual antiplatelet agents which can pose high bleeding risk (need additional ref here).

There are limitations associated with this study. Firstly, our primary endpoints were observed at 30 days, which is a relatively short period. A similar analysis we performed for outcomes at 1-year also found no differences in outcomes between AC and no-AC groups, but the analysis suffered from poor follow up, thereby limiting its reliability results. Second, our small sample size and number of events may preclude our ability to truly characterize outcomes. Despite propensity score matching, the retrospective nature of our study may fail to capture key variables related to patient selection and may thus cofound outcomes. Given the lack of standardized protocols for LAAL and AC utilization in our cohort, there is also a small risk of selection bias. In addition, we cannot confirm compliance for patients who were prescribed DOACs, or for those on

warfarin who underwent INR monitoring outside of our institution's network. Missing data, particularly in the setting of chart review and follow-up phone calls, may underestimate or overestimate the frequency of adverse events within the total study population. The cumulative incidence of stroke at 30 days in patients who underwent LAAL and received AC is elevated at 0.1%, which may suggest selection bias towards high-risk patients. Postoperative AC utilization following CABG may have been influenced by the presence of dual antiplatelet therapy. Late migration or dislodgement of the closure devices have previously been reported [29] [32], which cannot be ruled out in patients who lack long-term echocardiographic follow-up. Furthermore, lack of ECG data at 30 days follow-up limits our understanding of the contribution of postoperative cardiac rhythm changes to patient outcome, and the overall short follow-up and small sample size for our study necessitates further analysis with longer-term outcomes.

5. Conclusion

Our retrospective study suggests that patients with an elevated CHA_2DS_2-VASc score who undergo epicardial LAAL and are not treated with AC at the time of their hospital discharge demonstrate no difference in post-discharge stroke, mortality, nor in major bleeding rate at 30 day follow-up. Systemic AC is not without risks, particularly in our increasingly elderly population, and further prospective studies are warranted to better characterize both the guidelines for interventional stroke prophylaxis in patients with AF, as well the indications for surgical LAAL in patients without AF.

Author Contribution Statement

Alexander P Kossar: Conceptualization; Data curation; Investigation; Methodology; Supervision; Writing—Original Draft; Writing—review & editing. Yaagnik D Kosuri: Data curation; Formal Analysis; Investigation; Methodology; Writing—original draft; Writing; review & editing. Samantha Nemeth: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Writing—original draft; Writing—review & editing. Brigitte E. Kazzi: Conceptualization; Data curation; Investigation; Writing—original draft. YumingNing: Data curation; Formal analysis; Methodology; Validation. James Doolittle: Data curation; Investigation; Methodology; Resources. Denise McLaughlin: Data curation; Investigation; Methodology; Resources. Paul Kurlansky: Conceptualization; Data curation; Investigation; Methodology; Supervision; Formal Analysis; Writing—Original Draft; Writing—review & editing. Isaac George: Conceptualization; Data curation; Investigation; Methodology; Supervision; Formal Analysis; Writing—Original Draft; Writing—review & editing.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Supplemental Appendix 1

- CVD includes the following field options which have changed on the data collection form over time: CVD, TIA, neurological event, or procedure for CVD.
- Shock included the following field options which changed on the data collection form over time: hemodynamically unstable at time of procedure, hemodynamic shock at time of procedure, cardiogenic shock, refractory shock.
- CHF included both current and past CHF.
- Surgical priority was condensed to elective vs. not elective.
- Previous MI combined all field options for any MI within the past 21 days.
- 3 patients had an outcome (2 stroke, 1 bleed) but date was unknown so it was determined to be on day 0.
- Patients marked unknown to outcomes (8) were considered not to have it.

Table S1. Unknown data points.

Field	N	Remediation
Creatinine	1 Missing	Imputed via Random Forest Multiple Imputation
Ethnicity	4 Unknown	Imputed via Random Forest Multiple Imputation
Race	4 Unknown	Imputed via Random Forest Multiple Imputation

Table S2. Definitions.

Field	Remediation
Aorta	If the patient had an aorta procedure with or without another concomitant procedure
Total CABG	If the patient had an Isolated CABG or a CABG + Other procedure (excluding Aorta)
Total Valve	If the patient had an isolated valve or a Valve + Other procedure (excluding Aorta)
Total Valve/CABG	If the patient had a CABG + Valve procedure with or without an Other procedure done concomitantly

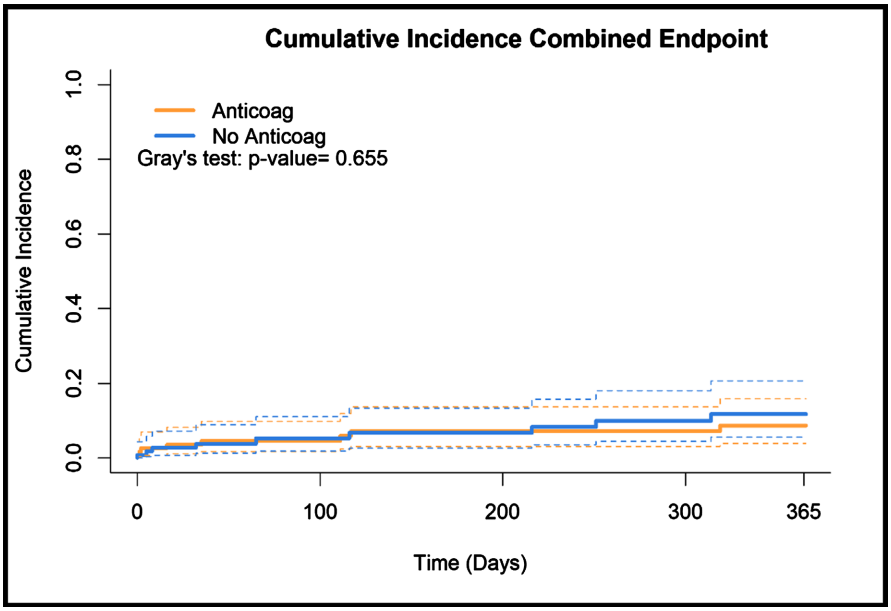
Table S3. Outcomes for the matched study cohort.

	Number of 1-year Outcomes	Number of Competing Events (death) prior to outcome	Cumulative Incidence at 1 year	CI	P-value
Stroke*					0.400
Anticoagulant	3	1	0.035	[0.009 - 0.093]	
No Anticoagulant	5	2	0.067	[0.024 - 0.141]	
Postoperative Bleeding*					0.727
Anticoagulant	3	1	0.027	[0.007 - 0.070]	
No Anticoagulant	2	2	0.028	[0.005 - 0.093]	

Continued

Readmission for Cardiac Re-Intervention*					0.348
Anticoagulant	1	1	0.013	[0.001 - 0.062]	
No Anticoagulant	0	2	0	[NA]	
Mortality					0.495
Anticoagulant	1	NA	0.013	[0.001 - 0.062]	
No Anticoagulant	2	NA	0.023	[0.004 - 0.075]	
Composite Outcome					0.655
Anticoagulant	8	NA	0.088	[0.040 - 0.159]	
No Anticoagulant	9	NA	0.118	[0.056 - 0.206]	

*Used Fine and Gray competing risk.



Legend: Cumulative one-year incidence of the composite endpoint in patients who underwent left atrial appendage ligation and were discharged with or without anticoagulation.

Figure S1. Cumulative incidence of the composite outcome.

Table S4. Mortality follow-up (n = 479).

	No Follow Up (n = 247)	Follow Up (n = 232)	p value
Age	70 (64, 76.5)	70 (63, 76)	0.39
BMI	28.1 (24.8, 32.7)	27.3 (24.4, 31.2)	0.12
Creatinine	1.09 (0.88, 1.29)	1.03 (0.90, 1.21)	0.41
CHAD	4 (3, 6)	4 (3, 5)	0.53
EF	58 (50.5, 63)	55 (49.8, 63)	0.05
Female	95 (38.5)	81 (34.9)	0.48

Continued

Hispanic	34 (13.9)	33 (14.3)	0.99
Preop_afib	102 (41.3)	125 (53.9)	0.008
Postop_afib	155 (62.8)	157 (67.7)	0.3
Procedure			
Aorta	32 (13)	44 (19)	
V	107 (43.3)	105 (45.3)	
C	61 (24.7)	39 (16.8)	
V/C	47 (19)	44 (19)	
Elective	**174 (70.4)**	**116 (50)**	**<0.001**
Diabetes	**83 (33.6)**	**53 (22.8)**	**0.01**
Renal Failure	245 (100)	227 (100)	NA
CVD	44 (17.8)	48 (20.7)	
CLD	**25 (10.1)**	**48 (20.7)**	**0.002**
PVD	32 (13)	53 (22.8)	0.007
HTN	211 (85.4)	185 (79.7)	0.13
CHF	115 (46.6)	108 (46.6)	1
Pre_Organ_Tx	244 (100)	229 (100)	NA
Pre_MI	188 (76.1)	191 (82.3)	0.12
Pre_Surgery	11 (4.5)	19 (8.2)	0.13
ConComitant	**78 (31.6)**	**98 (42.2)**	**0.02**

Table S5. Stroke Follow-Up (n = 479).

	No Follow Up (n = 251)	**Follow Up (n = 228)**	**p value**
Age	70 (64, 76)	70 (63, 76)	0.52
BMI	28.1 (24.8, 32.8)	27.3 (24.4, 31.2)	0.11
Creatinine	1.10 (0.88, 1.29)	1.02 (0.90, 1.21)	0.37
CHAD	4 (3, 6)	4 (3, 5)	0.6
EF	57 (50.5, 63)	55 (49.8, 63)	0.07
Female	97 (38.6)	79 (34.6)	0.42
Hispanic	34 (13.7)	33 (14.6)	0.87
Preop_afib	**105 (41.8)**	**122 (53.5)**	**0.01**
	158 (62.9)	154 (67.5)	0.34
Procedure			
Aorta	32 (12.7)	44 (19.3)	
V	109 (43.4)	103 (45.2)	

Continued

C	62 (24.7)	38 (16.7)	
V/C	48 (19.1)	43 (18.9)	
Elective	**177 (70.5)**	**113 (49.6)**	**<0.001**
Diabetes	**84 (33.5)**	**52 (22.8)**	**0.01**
Renal Failure	249 (100)	223 (100)	NA
CVD	45 (17.9)	47 (20.6)	0.53
CLD	**26 (10.4)**	**47 (20.6)**	**0.003**
PVD	33 (13.1)	52 (22.8)	0.008
HTN	214 (85.3)	182 (79.8)	0.15
CHF	116 (46.2)	107 (46.9)	0.95
Pre_Organ_Tx	248 (100)	225 (100)	NA
Pre_MI	191 (76.1)	188 (82.5)	0.11
Pre_Surgery	13 (5.2)	17 (7.52)	0.4
ConComitant	**81 (32.3)**	**95 (41.7)**	**0.04**

Table S6. ReAdmission Follow-Up (n = 479).

	No Follow Up (n = 251)	**Follow Up (n = 228)**	**p value**
Age	70 (64, 76)	70 (63, 76)	0.52
BMI	28.1 (24.8, 32.8)	27.3 (24.4, 31.2)	0.11
Creatinine	1.10 (0.88, 1.29)	1.02 (0.90, 1.21)	0.37
CHAD	4 (3, 6)	4 (3, 5)	0.6
EF	57 (50.5, 63)	55 (49.8, 63)	0.07
Female	97 (38.6)	79 (34.6)	0.42
Hispanic	34 (13.7)	33 (14.6)	0.87
Preop_afib	**105 (41.8)**	**122 (53.5)**	**0.01**
	158 (62.9)	154 (67.5)	0.34
Procedure			0.07
Aorta	32 (12.7)	44 (19.3)	
V	109 (43.4)	103 (45.2)	
C	62 (24.7)	38 (16.7)	
V/C	48 (19.1)	43 (18.9)	
Elective	**177 (70.5)**	**113 (49.6)**	**<0.001**
Diabetes	**84 (33.5)**	**52 (22.8)**	**0.01**
Renal Failure	249 (100)	223 (100)	NA
CVD	45 (17.9)	47 (20.6)	0.53

Continued

CLD	**26 (10.4)**	**47 (20.6)**	**0.003**
PVD	33 (13.1)	52 (22.8)	0.008
HTN	214 (85.3)	182 (79.8)	0.15
CHF	116 (46.2)	107 (46.9)	0.95
Pre_Organ_Tx	248 (100)	225 (100)	NA
Pre_MI	191 (76.1)	188 (82.5)	0.11
Pre_Surgery	13 (5.2)	17 (7.52)	0.4
ConComitant	**81 (32.3)**	**95 (41.7)**	**0.04**