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Copyright© 2013-21 IJDRA**Research Article****Low Embolic Risk from Short Duration Atrial Fibrillation following Anatomic Lung Resection****Boxiang Jiang^a, Philip Linden^a, Alejandro Oliu^b, Christopher Towe^a, Yaron Perry^c, Stephanie Worrell^{*a}**^aUniversity Hospitals Cleveland Medical Center, Department of Surgery, Division of Thoracic Surgery, 11100 Euclid Avenue, Cleveland, OH 44106^bCarle Foundation Hospital, Department of General Surgery, 511 W. Part St., Urbana, IL 61802^cState University of New York, University at Buffalo, Jacobs School of Medicine and Biomedical Sciences, Division of Thoracic Surgery, 100 High Street, Buffalo, NY 14203**Abstract****Objectives**

There is no consensus regarding the merits of anticoagulation following short duration atrial arrhythmia and anatomic lung resection. We hypothesized that the risk of embolic event following episodes of atrial fibrillation (AF) lasting less than 48 hours is low and even with an elevated CHA2DS2-VASC score should not incur the risk of long-term full dose anticoagulation contrary to recommendations.

Design & Intervention

A retrospective review was performed of a prospectively maintained database of all patients undergoing anatomic lung resection at a single institution from 2014 to 2019. Patients who had new onset post-operative atrial fibrillation (POAF) were queried as to their comorbidities, the length of arrhythmia, discharge with anticoagulation, and any post-operative embolic events.

Main Outcome Measures

There were 565 patients who underwent anatomic lung resection. 40 patients (7.1%) developed new POAF that lasted a median of one day. In 32 patients (80%), POAF lasted for less than 48 hours. There were 28 males and 12 females, median age of 73 years. These patients underwent segmentectomy (2/40), lobectomy (24/40) and pneumonectomy (14/40). Twenty-nine patients were discharged home without anticoagulation. Median follow-up was 22 month (range 1.3 – 62.8 month). Two patients had embolic events and these two were discharged home without anticoagulation. The overall incidence rate of thromboembolic events was 3.2% per person year.

Conclusions

Our data suggest that the risk of arterial embolic events is low in patients with new, short duration atrial fibrillation post anatomical lung resection. Anticoagulation may not be necessary in these patients and can be given selectively.

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1. Introduction

Atrial fibrillation (AF) after anatomical lung resection is a frequent post-operative complication occurring in 12-20% of patients. (1,2) Post-operative AF (POAF) occurs most commonly during the first two postoperative days (POD). (2) The known risk factors for POAF include a prior history of paroxysmal AF, heart failure, male gender, advanced age and increased

extent of resection. (3) POAF is usually transient and self-resolving. However, it is often an indicator of a complex post-operative course. (1,2) The treatment of POAF includes assessment of hemodynamic stability and either rate or rhythm control. (1) However, there is no consensus on the use of anticoagulation in short-duration AF to prevent future thromboembolic event following anatomical lung resection.

The 2014 American Heart Association (AHA) and American College of Cardiology (ACC) guidelines state that it is reasonable to start antithrombotic agents to treat POAF in patient undergoing cardiac and thoracic surgery. (4) This statement was purposefully vague due to the lack of robust clinical evidence. (4) Society of Thoracic Surgery (STS) guideline recommended AC for POAF that lasted longer than 48 hours with two or more risk factors for strokes but did not have recommendation for PAF that lasted less than 48 hours. (5) American Association for Thoracic Surgery (AATS) recommended AC for POAF that lasted longer than 48 hours. (6) AATS further recommended AC for POAF lasted less than 48 hours with a CHA₂DS₂-VASC score of 2 or higher. (6) We proposed that the embolic risk following post anatomic lung resection AF lasting for less than 48 hours was low and even with an elevated CHA₂DS₂-VASC score should not incur the risk of long-term full does anticoagulation contrary to recommendations.

2. Material and Methods

Patient Population

A retrospective chart review of a single academic center database was completed for all patients undergoing anatomic lung resection from 2014 to 2019. Anatomical lung resections included pneumonectomy, bi-lobectomy, lobectomy, and segmentectomy. Patients that underwent a wedge resection were excluded. Patient comorbidities, operation details and postoperative outcomes were queried. Patients who developed new POAF were identified. Patients who had chronic AF prior to the operation were excluded.

POAF

POAF was identified by reviewing documentations and EKG records in the electric medical record (EMR). The starting time of AF was calculated from the time of surgery. The duration of POAF was recorded. The CHA₂DS₂-VASC scores were calculated from patients' comorbidities. Anticoagulation information was recorded if patients were started on anticoagulation prior to discharge from the hospital.

Follow-up and Embolic Events

Any post-operative embolic event was identified by reviewing in-patient and out-patient EMR. Embolic events were identified as transient ischemic attack (TIA),

ischemic strokes, limb ischemia, or mesentery ischemia. Major bleeding events on people who were discharged on anticoagulation were also identified. We followed all the patients to their last documentation in the EMR.

Statistics

Demographic and clinical differences between the groups of patients with POAF and those without AF were described using mean and standard deviation for continuous variables and frequency and percentages for categorical variables. Comparison of groups was performed using Wilcoxon rank sum for continuous variables and chi-square for categorical data. The study was approved by the Case Western Reserve University IRB committee. This work was supported by University Hospitals Research in Surgical Outcomes & Effectiveness Center (UHRISES).

3. Results

Patient Population

There were 565 patients who underwent anatomical lung resection from 2014 to 2019. Among these patients, there were eight patients with chronic paroxysmal AF who were excluded from the analysis. Forty patients (7.2%) developed new-onset POAF. The selection and treatment of these patients were demonstrated in Figure 1. The characteristics and co-morbidities of the remaining 557 patients were summarized in Table 1. Patients who developed new POAF were significantly older, taller and were more likely to undergo a pneumonectomy and receive neoadjuvant radiation therapy (Table 1). New POAF was also associated with a significantly longer hospital stay. The length of stay for POAF patients was increased by an average of three days compared to patients who did not develop POAF (Table 2). Patients with new POAF had a significantly higher rate of postoperative complications (Table 2). Patients with new POAF had higher rate of urinary tract infection (5% vs 1.2%, $P = 0.056$) and atelectasis (7.5% vs 2.13%, $P = 0.046$). Patients with new POAF required a significantly higher number of transfusions and had more unexpected transfers to the ICU compared to patients without POAF (Table 2). There was no significant difference in 30-day mortality, between new POAF patients and no POAF patients (0% vs. 0.58%, $P = 0.6$).

Table 1. Patient Characteristics and Co-Morbidities. (* indicates statistical significance)

Parameter	POAF	No POAF	P value
Total Patients	40	517	-
Operations			
Pneumonectomy	14 (35%)	35 (6.8%)	<0.001*
Bi-lobectomies	3 (7.5%)	24 (4.6%)	0.45
Lobectomy	21 (52.5%)	420 (81.2%)	0.11
Segmentectomy	2 (5%)	38 (7.4%)	0.62
Age (year)	73.0	67.9	0.02*
Gender (% male)	28 (70%)	220 (43%)	0.05*
Height (cm)	175.47	167.05	<0.001*
Weight (kg)	80.72	77.00	0.26
BMI	25.76	26.73	0.07

Hypertension	24 (60%)	318 (61.5%)	0.94
CHF	1 (2.5%)	27 (5.3%)	0.46
CAD	8 (20%)	94 (18.2%)	0.81
CVA			
Never	38 (95%)	478 (92.5)	0.91
Irreversible Deficits	1 (2.5%)	24 (4.6%)	0.57
Reversible Deficits	1 (2.5%)	13 (2.5%)	0.99
DM	7 (17.5)	80 (15.5%)	0.76
Neoadjuvant radiation	8 (20%)	39 (7.5%)	0.02*
Neoadjuvant chemotherapy	8 (20%)	90 (17.4%)	0.75
Smoking Status			
Never	5 (12.5%)	84 (16.2%)	0.60
Former	24 (60%)	258 (49.9%)	0.49
Current	10 (25%)	175 (33.8%)	0.40

Acronyms: POAF = post-operative atrial fibrillation, BMI = body mass index, CHF = congested heart failure, CAD = coronary artery disease, CVA = cerebrovascular accident, DM = Diabetes Mellitus.

Table 2. Comparing Postoperative Complications between POAF and no POAF patients. (* indicates statistical significance)

Parameter	POAF	No POAF	P Value
Total Patients	40	517	
LOS (median days)	6	3	<0.001*
Airleak	1 (2.50%)	39 (7.54%)	0.27
Atelectasis	3 (7.50%)	11 (2.13%)	0.05*
Pneumonia	2 (5.00%)	9 (1.74%)	0.17
Empyema	1 (2.50%)	4 (0.77%)	0.27
ARDS	0	1 (0.19%)	0.78
BPF	0	4 (0.77%)	0.58
DVT	0	3 (0.58%)	0.63
PE	0	2 (0.39%)	0.69
Ileus	0	1 (0.19%)	0.78
C. Difficile infection	0	1 (0.19%)	0.78
Transfusion	4 (10.00%)	14 (2.71%)	0.02*
UTI	2 (5.00%)	6 (1.16%)	0.06
SSI	0	1 (0.19%)	0.78
Sepsis	0	1 (0.19%)	0.78
Other infection	1 (2.50%)	2 (0.39%)	0.08
Unexpected admission to ICU	3 (7.50%)	8 (1.55%)	0.01*
30-day mortality	0	3 (0.58%)	0.63

Acronyms: POAF = post-operative atrial fibrillation, LOS = length of stay, ARDS = Acute Respiratory Distress Syndrome, BPF = Bronchopleural Fistula, DVT = Deep Vein Thrombosis, PE = Pulmonary Embolism, UTI = Urinary Tract Infection, SSI = Surgical Site Infection, ICU = Intensive Care Unit

New POAF

Forty patients developed new POAF and 32 (80%) had POAF that lasted less than 48 hour (Figure 1). The median duration of POAF was 24 hrs, with the longest episode lasting 6 days. The median time to onset was POD 2. The majority (85%) of POAF episodes started within the first 72 hours following surgery (Figure 2). Patients (7.5%) were unlikely to develop new-onset POAF after POD4 (Figure 2). Two patients with new onset AF were discharged home in rate-controlled AF and fully anticoagulated. All other patients converted to sinus rhythm prior to discharge from the hospital and all patients had converted to sinus rhythm by the time they returned for their first post-operative clinic appointment. The median CHA₂DS₂-VASc score was 2.5 (ranging from 0 to 6) and thirty patients (75%) had CHA₂DS₂-VASc score of 2 or higher. Eighteen patients (45%) had

two or more risk factors for stroke per STS guidelines (age >75 years, hypertension, impaired left ventricular function, history of stroke). (5) Ten patients were discharged home with anticoagulation (AC) and the remaining 30 patients were not (Figure 1). Among the 10 patients, seven patients were discharged home on warfarin, two on apixaban, and one on enoxaparin. Compared to patients who were discharged home without AC, patients who were discharged with AC had significantly longer duration of POAF (3.20 vs. 1.43 days, p = 0.005). The CHA₂DS₂-VASc scores were comparable between these two groups (Table 3). Of 10 patients discharged with AC, one patient (10%) had one major hemorrhagic episode during an unrelated outpatient endoscopic procedure. This patient required a blood transfusion and an unexpected ICU admission. This patient eventually recovered, and warfarin was re-

started without further issue. The incidence of major hemorrhage for patients on AC was 5.2%/person-year.

Embolic Events

At a median follow-up of 22 months (range from 1.3 to 62.8 month) there were two patients that had an embolic event. Both events occurred in patients who were discharged home without AC. The incidence of all embolic events was 3.2% per person-year and 1.6% per person-year for ischemic stroke alone (Table 3). Patient A suffered an acute limb ischemia requiring emergent

embolectomy. This occurred within two days of discharge from the hospital. The patient recovered without complication. Patient B suffered an ischemic stroke 57 days following discharge from the hospital. This patient also recovered with no residual neurological deficit. Both patients had short duration POAF that converted to sinus rhythm in less than 48 hours. Their CHA₂DS₂-VASc scores were 3 and 0 for patient A and B, respectively.

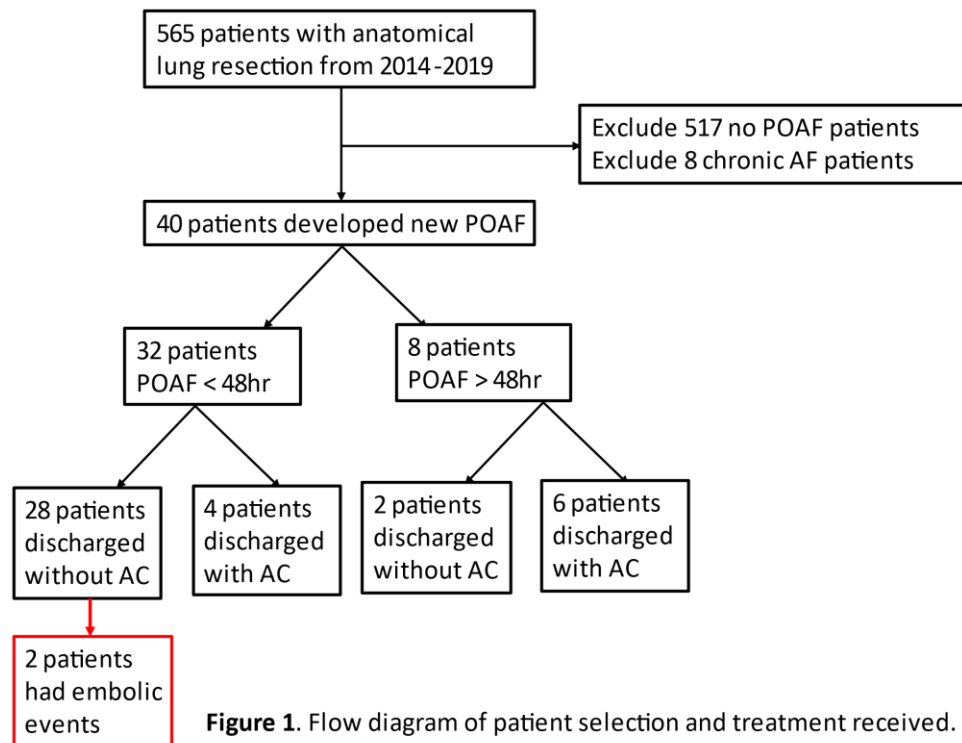


Figure 1. Flow diagram of patient selection and treatment received.

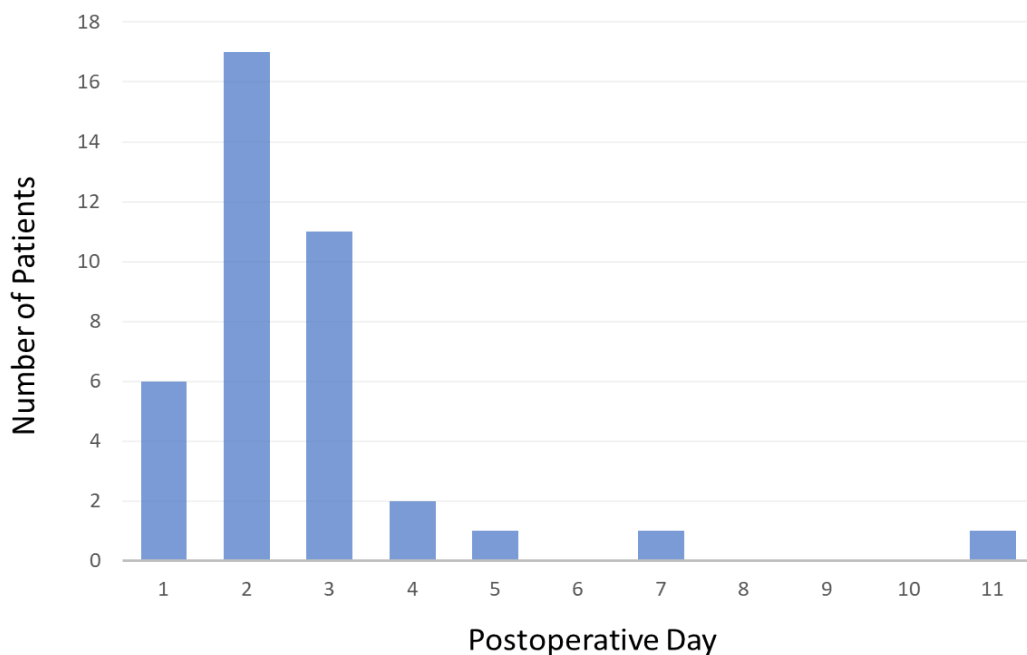


Figure 2. Timing of POAF. Plotted as number of patients vs. postoperative day of POAF onset.

Table 3. POAF Patients characteristics and a comparison between patients who discharged with AC and without AC. (* indicates statistical significance)

POAF Patients Characteristics			
Average time of onset (POD#)	2		
Duration (day)	1 (1 - 6)		
CHA ₂ DS ₂ -VASC score average	2.68 (+/- 1.72)		
Embolic events	2		
Length of follow-up (month)	24.49 (1.3 – 62.8)		
Incidence of embolic events on patients without AC (events/person-year)	3.2%		
Incidence of ischemic stroke on patients without AC (events/person-year)	1.6%		
Major hemorrhage events	1		
Incidence of major hemorrhage on patients with AC (events/person-year)	5.2%		
Patients discharged without AC vs with AC			
Parameter	No AC	On AC	P value
Number of Patients	30 (75%)	10 (25%)	n/a
Duration of POAF (days)	1.43	3.20	<0.01*
CHA ₂ DS ₂ -VASC score	2.7	2.6	0.93
Length of follow-up (month)	25	23	0.91
Embolic events	2	0	0.39
Major hemorrhagic events	0	1	0.09

Acronyms: POAF = postoperative atrial fibrillation, AC = anticoagulation, POD = Postoperative day

4. Discussion

POAF after anatomical lung resection is a known and not infrequent complication. (2) POAF is usually transient and self-limiting. (2) It, however, is not a benign complication. Literature supports that POAF after lung resection is associated with a higher rate of complications and prolonged hospital course. (1,2) This was also demonstrated in our study, with patients who developed POAF having significantly longer hospital stays and an increased rate of post-operative complications. These patients also had a significantly higher rate of blood transfusions and ICU admissions. This finding was consistent with prior study showing that blood transfusion was an independent predictor of POAF. (7) POAF is readily managed with rate and/or rhythm control medications. However, the need for long term anticoagulation to prevent thromboembolic events after short duration transient POAF is still controversial.

In the 2014 AHA/ACC guidelines for AF management, it is recommended to start antithrombotic therapy for all patients who developed AF after cardiac or thoracic surgery. (4) This recommendation is based on a single study of AF after coronary artery bypass surgery. (4) STS guideline recommended AC for POAF that lasted longer than 48 hours with two or more risk factors for strokes but did not have any recommendation for POAF less than 48 hours. (5) AATS recommended AC for POAF that lasted less than 48 hours with a CHA₂DS₂-VASC score of 2 or higher. (6) In our cohort, 30 POAF patients (75%) had CHA₂DS₂-VASC score of 2 or higher and only 7 patients (of 30) received AC post discharge. M. Garner et al reported that only three patients (7%) in their cohort of 43 transient POAF patients received long term AC. (8) No study has been done to delineate the rate of thromboembolic events after

post-anatomical lung resection short duration transient AF. Our study was the first to report a low thromboembolic rate in this patient population. The incidence rate of 3.2% of all thromboembolic events was comparable to a CHA₂DS₂-VASC score between 2 and 3 in medical AF patients. The ischemic stroke in our study was 1.6% which was less than that predicted by CHA₂DS₂-VASC score (2.5-3.7%/person year). (9) The thromboembolic rate and ischemic stroke rate were low but not completely neglectable in this study. Both events occurred in the post-operative period (less than 90 days). The two patients who developed thromboembolic events had transient, self-limiting POAF. Interestingly, the CHA₂DS₂-VASC score of the ischemic stroke patient was 0 at discharge. This patient would not receive AC according to AATS or STS guideline. It was not clear that both thromboembolic events were related to POAF or other underlying comorbidities. We did not perform routine echocardiogram for patients with POAF less than 48 hours prior to discharge. It is also possible that they developed recurrent AF after discharge, leading to the thromboembolic event. However, in our series of 40 patients, recurrent AF after initial POAF was not observed during their follow up appointments. However, we did not have the ability to perform continuous cardiac monitor after discharge. For patients who were discharged home with AC, warfarin was still the first choice for the majority of physicians. In medical AF, warfarin significantly increases the risk of extracranial bleeding by 70%. (10) In our post-anatomical lung resection patient population, the risk of hemorrhage risk was a significant concern. Sixty percent of our patients have hypertension and the majority are over the age of 65 years. These two factors are known to increase the risk for major bleeding. (11) Committing these lung resection patients to AC for transient POAF may cause

more harm than benefit. In our study, 10% of the patients who were started on AC developed a major hemorrhagic event. The incidence of hemorrhage was greater than that of thromboembolic event in our series.

Our study has several limitations. This study is a small sample from a single tertiary care institution. This was a retrospective review with no control group. We had a limited number of patients which made observation rate of thromboembolic and hemorrhagic events rare. This study was underpowered to either recommend for or against anticoagulation use for short term POAF. The reason to initiate or withhold AC in our series was not always clear. This decision was made based on individual surgeon preference. This reflects a lack of consensus of treating POAF in this patient population. Additionally, we were unable to monitor patients for recurrent atrial fibrillation beyond discharge and the post-operative clinic visit, which might have led to missed post-discharge atrial fibrillations.

5. Conclusion

Post-anatomical lung resection AF that lasts less than 48 hours has a low thromboembolic risk and the risks and benefits of long-term anticoagulation therapy should be weighed for each individual patient. A multi-institutional study should be conducted to further delineate the risk and benefit of starting AC on this patient population.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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