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Original research article

A RETROSPECTIVE OBSERVATIONAL RESEARCH TO ASSESS THE INCIDENCE OF ACUTE ISCHEMIC STROKE IN HOSPITALIZED ATRIAL FIBRILLATION PATIENTS WITH ANTICOAGULATION INTERRUPTIONS

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Abstract

Aim: To determine the Incidence of Acute Ischemic Stroke in Hospitalized Patients with Atrial Fibrillation Who Had Anticoagulation Interruption.
Methods: A retrospective study was conducted in the Department of Cardiology This study included patients 18 years or older who were admitted to the hospital with a primary or secondary diagnosis of AF who had anticoagulation interruption without heparin bridge vs. non-interrupted group.
Results: A total of 450 patients were included in the study. In this cohort, mean age was 71.1 ± 10.21 years and 50.89% were female. A total of 50 patients out of 450 (11.11%) had anticoagulation interruption in more than 48 h (median interruption of 67 h). Compared to non-interruption group, patients with anticoagulation interruption were older (mean age 75.45 ± 10.52 vs. 71.06 ± 10.88 years, P = 0.001), had slightly higher $CHADS_2VASc$ score (3.88 vs. 3.52, P = 0.01), more likely to have heart failure and less likely to have HTN. Only 10 patients out of 450 (2.22%) had acute ischemic stroke during their hospital stay: 2 patient (4%) in the anticoagulation interruption group, and 8 patients (2%) in the non-interruption group. There was no statistically significant difference in incidence of ischemic stroke between the two groups (1.31% vs. 0.27%, P = 0.21). Short-term interruption of anticoagulation was not associated with a significant increased risk of in-hospital ischemic stroke. CHA_2DS_2VASc score was an independent strong predictor of in-hospital stroke (odds ratio (OR): 7.67, 95% confidence interval (CI): 2.89 - 18.03) In terms of secondary outcomes in anticoagulation interruption versus non-interruption groups, results were as follows: mortality (0 vs. 0.68%, P = 1), bleeding (4% vs. 1%, P = 0.03), number of readmissions within 90 days (48% vs. 37%, P = 0.03) and average LOS (7.74 vs. 2.75 days, P < 0.0001).
Conclusion: Patients suffering with AF the incidence of ischemic stroke during hospitalisation is minimal and does not rise considerably when anticoagulation is stopped for a short period of time. The CHA2DS2VASc score has a significant correlation with the occurrence of ischemic stroke in hospitalised patients with AF.
Keywords: ischemic stroke, anticoagulation, AF

Introduction

Atrial fibrillation (AF) raises the risk of a cerebrovascular event (CVE) by up to fivefold [1]. Patients with AF with a history of stroke are more likely to die, have heart failure, and have long-term impairment. Catheter ablation is the usual method for treating individuals with AF, and current research suggests that it may lower the risk of thromboembolism even more [2-4]. Current recommendations for antithrombotic treatment following catheter ablation for AF advocate ongoing oral anticoagulation (OAC) medication for all patients depending on the CHA2DS2-VASc risk profile [5]. However, in clinical practice, OAC therapy has been discontinued for many patients with a low-risk profile for thromboembolism. Very few studies have described outcomes in high-risk patients with apparently successful AF ablation following discontinuation of OAC therapy. Furthermore, these studies did not provide details of the type of stroke experienced (i.e., whether past CVEs were cardiogenic embolisms). We hypothesized that different subtypes of ischemic stroke may present different risk factors, clinical features and prognosis; therefore, the best post-procedural antithrombotic management for AF ablation may differ in patients with prior

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cardioembolic (CE) stroke and prior non-CE (i.e., non-AF related) stroke. Although risk of ischemic stroke among patients with AF during sepsis exceeds the risks of both the general population with AF and patients with sepsis who do not experience AF,[6] little evidence exists to support the use of anticoagulation for prophylaxis of arterial thromboembolism for patients with AF during sepsis [7, 8]. Management decisions regarding the use of anticoagulation for prophylaxis of arterial thromboembolism during sepsis are complicated by changes to the coagulation cascade and acute organ dysfunction that may increase risks of bleeding and thrombosis [9].

Materials and methods

A retrospective study was conducted in the Department of Cardiology, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or the relatives.

Methodology

The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients. Patients with a primary or secondary diagnosis of AF were included in this study. We included patients 18 years or older who were admitted to the hospital with a primary or secondary diagnosis of AF who had anticoagulation interruption without heparin bridge vs. non-interrupted group. We excluded patients who had acute ischemic cerebrovascular accident (CVA), hemorrhagic CVA, mechanical heart valves, previous or current deep vein thrombosis or pulmonary embolism on admission.

Statistical analysis

Baseline characteristics and outcomes were summarized by frequency tabulation and means with standard deviations as appropriate to compare patients with anticoagulation interruption vs. no interruption. T-tests were used to test for differences in-group means. Chi-square and Fisher's exact tests were used to test for differences in categorical variables (Fisher's exact tests used when one group in the comparison has less than five observations). To further evaluate the effect of anticoagulation interruption on the incidence of ischemic stroke, it was adjusted to $CHADS_2VASc$ score in a logistic regression model.

Results

A total of 450 patients were included in the study. In this cohort, mean age was 71.1±10.21 years and 50.89% were female. A total of 50 patients out of 450 (11.11%) had anticoagulation interruption in more than 48 h (median interruption of 67 h). Compared to non-interruption group, patients with anticoagulation interruption were older (mean age 75.45±10.52 vs. 71.06±10.88 years, P = 0.001), had slightly higher $CHADS_2VASc$ score (3.88 vs. 3.52, P = 0.01), more likely to have heart failure and less likely to have HTN. Other characteristics and differences between anticoagulation interruption and non-interruption groups are summarized in Table 1.

Only 10 patients out of 450 (2.22%) had acute ischemic stroke during their hospital stay: 2 patient (4%) in the anticoagulation interruption group, and 8 patients (2%) in the non-interruption group. There was no statistically significant difference in incidence of ischemic stroke between the two groups (1.31% vs. 0.27%, P = 0.21) (Table 2).

Short-term interruption of anticoagulation was not associated with a significant increased risk of in-hospital ischemic stroke. CHA_2DS_2VASc score was an independent strong predictor of in-hospital stroke (odds ratio (OR): 7.67, 95% confidence interval (CI): 2.89-18.03) (Table 3). The risk of ischemic stroke increased significantly in the moderate and high risk CHA_2DS_2VASc categories (score $\geq$ 5), only one patient developed stroke in the anticoagulation interruption group and had a $CHADS_2VASc$ score $\geq$ 7. None of the patients in the low risk group CHA_2DS_2VASc < 5 had a stroke (Table 4).

In terms of secondary outcomes in anticoagulation interruption versus non-interruption groups, results were as follows: mortality (0 vs. 0.68%, P = 1), bleeding (4% vs. 1%, P = 0.03), number of readmissions within 90 days (48% vs. 37%, P = 0.03) and average LOS (7.74 vs. 2.75 days, P < 0.0001). There was a statistically significant difference between two groups in terms of bleeding, readmissions and average LOS. There was no difference in in-hospital mortality between the two groups.

Table 1: Patient Characteristics of Anticoagulation Interruption versus no Interruption Groups

Parameter	Anticoagulant interruption 48 h+ N=50	No anticoagulation interruption=400	P-value
Age (mean ± SD)	75.45 ± 10.52	71.06 ± 10.88	0.001
Male, n (%)	21 (42)	200 (50)	0.11
CHA2DS2VASc (mean ± SD)	3.88 ± 1.13	3.52 ± 1.23	0.01
Ischemic CVA, n (%)	2 (4)	8 (2)	0.25
CHF, n (%)	28 (56)	120 (30)	< 0.001
HTN, n (%)	20 (40)	272 (68)	0.001
Age ≥ 75 years, n (%)	32 (64)	188(47)	0.014
Age 65 - 74 years, n (%)	18 (36)	212 (53)	0.21
Diabetes, n (%)	13 (26)	120 (30)	0.57
Vascular disease, n (%)	23 (46)	176 (44)	0.61
Bleeding, n (%)	2 (4)	4 (1)	0.03

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Mortality, n (%)	0 (0)	2 (0.5)	1.00
Readmission within 90 days, n (%)	24 (48)	148 (37)	0.03
Average LOS (mean ± SD)	7.74 ± 4.78	2.75 ± 2.39	< 0.0001

SD: standard deviation; CVA: cerebrovascular accident; CHF: congestive heart failure; HTN: hypertension; LOS: length of hospital stay.

Table 2: Association of Selected Factors with Acute In-Hospital Ischemic Stroke in Hospitalized Patients with a History of AF

Variables	Ischemic CVA	No ischemic CVA	P-value
Age (mean ± SD)	75.45 ± 10.52 (N = 10)	71.06 ± 10.88 (N = 440)	0.19
Male, n (%)	3 (30)	212 (48.18)	0.61
Female, n (%)	7 (7)	228 (51.82)	0.61
CHA2DS2VASc (mean ± SD)	6.70 ± 0.87	3.52 ± 1.63	0.07
CHF, n (%)	2 (20)	140 (31.82)	0.62
HTN, n (%)	8 (80)	249 (56.59)	0.24
Age ≥ 75 years, n (%)	6 (60)	208(47.27)	0.45
Age 65-74 years, n (%)	4 (40)	145 (32.95)	1.11
Diabetes, n (%)	3 (30)	139 (31.59)	0.63
Vascular disease, n (%)	3 (30)	177 (40.23)	0.64
Anticoagulation interrupted, n (%)	2 (20)	18 (4.09)	0.17
No anticoagulation interruption, n (%)	8 (80)	422 (95.91)	0.17
Bleeding, n (%)	0 (0)	5 (1.14)	1.2
Mortality, n (%)	0 (0)	3 (0.68)	1.2
Readmission within 90 days, n (%)	6 (60)	148(33.64)	0.62
Average LOS (mean ± SD)	6.90±11.23	2.91±2.24	0.43

AF: atrial fibrillation; SD: standard deviation; CVA: cerebrovascular accident; CHF: congestive heart failure; HTN: hypertension; LOS: length of hospital stay.

Table 3: CHA_2DS_2VASc Significantly Associated With the Outcome Variable of In-Hospital CVA

Effect	Odds ratio		95% Confidence interval
Any interruption 48+ h (1: presence vs. 0: no presence)	4.51	0.49	45.12
CHA_2DS_2VASc	7.67	2.89	18.03

Patients with higher CHA2DS2VASc scores are more likely than those with lower CHA2DS2VASc scores to have an in-hospital CVA. CHA2DS2VASc: congestive heart failure/left ventricular dysfunction, hypertension, age > 75 (two points), diabetes mellitus, history of stroke/TIA or thromboembolism (two points), vascular disease (prior myocardial infarction, peripheral artery disease, aortic plaque), age 65-74, sex category. CVA: cerebrovascular accident; TIA: transient ischemic attack.

Table 4: Incidence of Acute Ischemic CVA in Relation to CHA_2DS_2VASc Risk Categories

CHA2DS2VASc risk groups	Acute ischemic CVA in patients with AC interruption	Acute ischemic CVA in patients without AC interruption	P value
Low risk (score of 0-4) (N = 354)	0/27 (0%)	0/327 (0%)	1.11
Intermediate risk (score of 5-6) (N = 70)	0/22 (0%)	1/48 (2.08%)	1.11
High risk (score ≥ 7) (N = 26)	1/1 (100%)	2/25 (8%)	0.14

There is not a significant difference in the number of people that had a stroke between interruption and non-interruption groups, within each CHA_2DS- 2VASc risk category. Majority of the patients who suffered stroke were in the intermediate and high-risk categories. CVA: cerebrovascular accident; AC: anticoagulation.

Discussion

The results of the study are important in two ways. First, previous studies have quantified 30-day and 1-year risk for is- chemic stroke [10-13], however, our study quantifies the short- term in-hospital risk of ischemic stroke in AF patients who are admitted to the hospital. This gives physicians more solid data to weigh risk versus benefit of interrupting anticoagulation in hospitalized patients with high bleeding risk. The CHA_2DS-2VASc score was formulated to predict the 1-year risk of is-chemic stroke and has not been validated to predict short-term outcomes. Our study supports the common practice of using CHA_2DS_2VASC score as a predictor of short-term ischemic stroke risk in hospitalized patients with AF. Second, our study included hospitalized patients with AF who had anticoagulation interruption for any reason. Most studies on anticoagulation interruption included patients undergoing elective procedures. The BRIDGE trial which was the first prospective multicenter randomized controlled trial of patients with AF undergoing procedures showed no significant difference between treatments interrupted group compared to non-interrupted group with regards to stroke, systemic thromboembolism or TIA at 30 days. In our study we included all patients who had their anticoagulation interrupted and not bridged with heparin regardless of the reason. We could not ascertain the specific reason for the interruption though due to limitation in the data extraction. The rate of ischemic events was similar to that seen in the BRIDGE trial which was 0.3-

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0.4% for arterial thrombotic events over 30 days [14, 15]. Our results are in line with current guidelines. In the 2017 ACC guidelines [16-18], the ACC estimates the peri-procedural risk in AF patients at 0.35% for 30 days (based on BRIDGE and ORBIT AF studies) and recommends estimating an individual's daily risk of stroke or TIA by dividing the annual stroke risk by 365 days [18-20]. However, this approach is taken from studies done in mostly intermediate risk patients undergoing elective procedures.

Our study adds to the current literature by providing the actual rate of stroke during hospitalization which is higher than what would be expected using the ACC method of estimation. Although the ACC recommends that patients at highest risk for thromboembolic events without excessive bleeding risk should consider bridging, it acknowledges that whether or not to bridge patients with AF and a high CHA_2DS_2VASc score remains unclear. However, based on available data, some physicians consider bridging anticoagulation for patients with a confirmed recent stroke. Our study results agree with the ACC guidelines. It shows that the risk of acute stroke in low risk patients (CHA_2DS- 2VASc < 5) is negligible and this population can be safely taken off anticoagulation. And all stroke cases occurred in intermediate or high-risk group. The lack of statistically significant difference in the incidence of stroke between the two groups in intermediate and high-risk patients is likely due to small number of events.

Conclusion

The current study indicated that in hospitalised patients with AF, the incidence of ischemic stroke during hospitalisation is minimal and does not rise significantly with short-term anticoagulant discontinuation. The CHA2DS2VASc score has a significant correlation with the occurrence of ischemic stroke in hospitalised patients with AF. More research is needed to determine the effect of anticoagulation interruption duration on stroke incidence in the high-risk category.

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