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Investigate the incidence of acute ischemic stroke in hospitalized patients with atrial fibrillation who had their anticoagulation stopped in a Tertiary Care Hospital in Gujarat, India.

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Abstract

Aim: To determine the Incidence of AcuteI schemic Stroke in Hospitalized Patients With Atrial Fibrillation Who Had Anticoagulation Interruption.

Methods: A comparative study was conducted in the Department of Medicine, Baroda Medical College and S.S.G. Hospital, Vadodara, Gujarat, India. This study included patients18yearsorolderwhowereadmittedtothehospitalwitha primary or secondary diagnosis of AF who had anticoagulation interruption without heparin bridge vs. non-interruptedgroup.

Results: The mean age of this cohort was 71.1 10.21 years, and 50.89 percent of the participants were female. A total of 50 patients (11.11 percent) out of 450 patients (450 patients) had their anticoagulation interrupted for more than 48 hours (median interruption of 67 h). Patients who had anticoagulation interruption were older (mean age 75.45 10.52 years vs. 71.06 10.88 years, P = 0.001), had a slightly higher CHADS2VASc score (3.88 vs. 3.52, P = 0.01), were more likely to have heart failure, and were less likely to have excessive blood pressure (P = 0.001). One in every 450 patients (2.22 percent) experienced an acute ischemic stroke during their hospitalisation, with only two patients (4 percent) in the anticoagulation interruption group and eight patients (2 percent) in the non-interruption group suffering from the condition. There was no statistically significant difference in the incidence of ischemic stroke between the two groups (1.31 percent vs. 0.27 percent, P = 0.21; 1.31 percent vs. 0.27 percent, P = 0.21; 1.31 percent vs. 0.27 percent, P = 0.21). The cessation of anticoagulation for a short period of time did not seem to be linked with a significantly higher risk of in-hospital ischemic stroke.

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Conclusion: The incidence of ischemic stroke in hospitalised patients with atrial fibrillation (AF) is low during hospitalisation and does not increase substantially with short-term anticoagulant cessation.

Keywords: schemicstroke, anticoagulation, AF

Introduction

Patients with atrial fibrillation (AF) have up to a fivefold increased risk of a cerebrovascular event (CVE).[1] Patients with AF who have previously had a stroke are more likely to die, suffer heart failure, and have permanent disability. In the general population, recent research indicates that catheter ablation may further reduce the incidence of thromboembolism even more.[2-4] For individuals with a CHA2DS2-VASc risk profile, current guidelines for antithrombotic therapy after catheter ablation for AF support continued oral anticoagulation (OAC) treatment for all patients.[5] However, OAC treatment is no longer in clinical practise due to the low-risk profile for thromboembolism of many individuals. Few studies have studied the effects of AF ablation in high-risk individuals who stop using OACs. Additionally, these investigations failed to provide information on the kind of stroke a person suffered from (ie, whether past CVEs were cardiogenic embolisms). In order to investigate whether the risk factors, clinical characteristics, and outcome of ischemic stroke varied depending on the presence of cardioembolic vs non-AF-related previous stroke, we developed a hypothesis and performed a research study. Despite the increased risk of ischemic stroke among individuals with AF during sepsis, data suggests that anticoagulation for the prevention of arterial thromboembolism is of limited benefit for these patients.[6-8] While alterations to the coagulation cascade and acute organ failure may raise risks of bleeding and thrombosis, management choices about the use of anticoagulation for prevention of arterial thromboembolism during sepsis are confounded by the complexity of this processes.[9]

Materials and methods

The present comparative studywas conducted in the DepartmentofMedicine, Baroda Medical College and S.S.G. Hospital, Vadodara, Gujarat, India. After taking the approval of the protocol review committee and institutional ethics committee and informed consent, detailed history was taken from the patient or the relatives.

Methodology

This research looked at patients with a main or secondary diagnosis of AF. Patients who had stopped anticoagulation without a heparin bridge, or interrupted anticoagulation and did not have a heparin bridge, were included in the study. This admission criteria excluded those patients who had a recent (within 1 month) or chronic (longer than 1 month) transient ischemic attack (TIA), had suffered an acute ischemic CVA (hemorrhagic or mechanical), or had undergone previous or current treatment for deep vein thrombosis or pulmonary embolism.

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Statisticalanalysis

Baseline characteristics and outcomes were tabulated and shown by means and standard deviations where applicable to compare patients who were interrupted in their anticoagulation treatment (anticoagulation interruption) to those who were not (no interruption). Student T-tests were performed to see if in-group means differed. Chi-square and Fisher's exact tests were used to determine if categorical variables varied (comparison groups had fewer than five observations and the Fisher's exact test was employed). The change to CHADS2VASc score in a logistic regression model was used to assess the additional impact of anticoagulation interruption on the incidence of ischemic stroke.

Results

The research comprised 450 participants. The mean age in this cohort was 71.1 years, with 50.89% of the individuals being female. There were 50 patients out of 450 (11.11% of the total) whose anticoagulant treatment was interrupted for more than 48 hours (median interruption of 67 h). Patients who experience anticoagulation interruption had significantly longer age (75.45 ± 10.52 years) and higher CHADS2VASc score (3.88 vs. 3.52, P = 0.01) than patients who did not experience interruption. In addition to differences outlined in Table 1, features and differences between the two groups of anticoagulation interruption and non-interruption are shown in the following table.

In the anticoagulation interruption group, two patients (4 percent) experienced acute ischemic stroke, whereas in the non-interruption group, eight patients (2 percent) had the condition. Incidence of ischemic stroke was not significantly different between the two groups (1.31% vs. 0.27%, P = 0.21). (Table 2).

There was no substantial increase in the risk of in-hospital ischemic stroke when anticoagulation was temporarily stopped. In-hospital stroke was a significant independent predictor of the CHA2DS2VASc score (OR: 7.67, 95% CI: 2.89 to 18.03). (Table 3). Moderate and high risk CHA2DS2VASc categories (score ≥ 5) led to a substantially higher risk of ischemic stroke, with just one patient experiencing a stroke during the anticoagulation interruption. In the low-risk group CHA2DS2VASc < 5, no individuals suffered a stroke (Table 4).

There were no significant differences between the two groups, in terms of secondary outcomes in anticoagulation interruption versus non-interruption groups. Mortality was 0 percent versus 0.68 percent in the intervention group, with a P value of 1; Bleeding was 4 percent versus 1 percent in the intervention group, with a P value of 0.03; the number of readmissions within 90 days was 48 percent versus 37 percent in the intervention group, with a P value of 0.03; and the mean LOS was 7.74 days versus 2.75 days in the intervention group, with a P value of <0.0001. The average length of stay and the rate of readmissions were different between the two groups. In-hospital mortality was the same across the two groups.

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Table1.PatientCharacteristicsofAnticoagulationInterruptionVersusNoInterruptionGroups

Parameter	**Anticoagulantinterruption48h+ N=50**	**Noanticoagulation 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
CHA_2DS_2VASc(mean± SD)	3.88 ± 1.13	3.52 ± 1.23	0.01
IschemicCVA,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
Age65 - 74years, n (%)	18 (36)	212 (53)	0.21
Diabetes,n(%)	13 (26)	120 (30)	0.57
Vasculardisease,n(%)	23 (46)	176 (44)	0.61
Bleeding, n (%)	2 (4)	4 (1)	0.03
Mortality,n(%)	0 (0)	2 (0.5)	1.00
Readmissionwithin90days,n (%)	24 (48)	148 (37)	0.03
AverageLOS(mean±SD)	7.74 ± 4.78	2.75 ± 2.39	< 0.0001

SD:standarddeviation;CVA:cerebrovascularaccident;CHF:congestiveheartfailure;HTN:hypertension;LOS:lengthofhospitalstay.

Table2. AssociationofSelectedFactorswithAcuteIn-HospitalIschemicStrokeinHospitalizedPatientsWithaHistoryofAF

Variables	**IschemicCVA**	**NoischemicCVA**	**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
CHA_2DS_2VASc(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
Age65 - 74years, n (%)	4 (40)	145 (32.95)	1.11
Diabetes,n(%)	3 (30)	139 (31.59)	0.63
Vasculardisease,n(%)	3 (30)	177 (40.23)	0.64
Anticoagulationinterrupted,n(%)	2 (20)	18 (4.09)	0.17
Noanticoagulation	8 (80)	422 (95.91)	0.17

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interruption, n (%)			
Bleeding, n (%)	0 (0)	5 (1.14)	1.2
Mortality,n(%)	0 (0)	3 (0.68)	1.2
Readmissionwithin90days,n (%)	6 (60)	148(33.64)	0.62
AverageLOS(mean±SD)	6.90 ± 11.23	2.91 ± 2.24	0.43

AF:atrialfibrillation;SD:standarddeviation;CVA:cerebrovascularaccident;CHF:congestiveheartfailure;HTN:hypertension;LOS:lengthofhospitalstay.

Table3.CHA_2DS_2VAScSignificantlyAssociatedWiththeOutcomeVariableofIn-HospitalCVA

Effect	**Odds ratio**		**95%Confidenceinterval**
Anyinterruption 48+ h (1: presencevs. 0: no presence)	4.51	0.49	45.12
CHA_2DS_2VASc	7.67	2.89	18.03

Patient's with higher CHA2DS2VASc scores are more likely to have an intra-hospital cerebral vascular accident (CVA) than those with lower CHA2DS2VASc scores. Diabetes mellitus, history of stroke/TIA/thromboembolism (two points), vascular disease (previous myocardial infarction, peripheral artery disease, aortic plaque), age 65 - 74, and sex category are all factors in the CHA2DS2VASc score. CVA stands for cerebrovascular accident, while TIA stands for transient ischemic attack.

Table4. IncidenceofAcuteIschemicCVAinRelationtoCHA_2DS_2VAScRiskCategories

CHA2DS2VASc riskgroups	**AcuteischemicCVAinpatientswithACinterruption**	**AcuteischemicCVAinpatients withoutACinterruption**	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
Highrisk (score≥ 7) (N= 26)	1/1 (100%)	2/25 (8%)	0.14

Within each CHA2DS- 2VASc risk category, there is no statistically significant difference in the number of individuals who had a stroke between the interruption and non-interruption groups, according to the findings. In the intermediate and high-risk groups, the vast majority of individuals who had a stroke fell into this category. CVA is for cerebrovascular accident, while AC stands for anticoagulation.

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Discussion

It is essential to note that the study's findings are significant in two respects. First and foremost, prior research has assessed the risk of is-chemic stroke between 30 days and one year.[10-13]; oOn the other hand, our research assesses the short-term in-hospital risk of ischemic stroke in patients with atrial fibrillation who are hospitalised to a medical centre. This provides doctors with more reliable information when weighing the risks and benefits of stopping anticoagulation in hospitalised patients who are at high risk of bleeding. In order to predict the 1-year risk of is-chemic stroke, the CHA2DS-2VASc score was developed; however, it has not been validated for predicting short-term outcomes. Our findings confirm the widespread practise of utilising the CHA2DS2VASC score as a predictor of short-term ischemic stroke risk in hospitalised patients with atrial fibrillation (AF) (CHA2DS2VASC score). Second, our research included individuals with atrial fibrillation who were admitted to the hospital and whose anticoagulation had been interrupted for any reason. Patients having elective operations were included in the majority of research on anticoagulation interruption. According to the results of the BRIDGE trial, which was the first prospective multicenter randomised controlled trial of patients with atrial fibrillation who underwent procedures, there was no statistically significant difference between the treatments interrupted group and the non-interrupted group in terms of stroke, systemic thromboembolism, or transient ischaemic attack (TIA) at 30 days. We included all patients who had their anticoagulation stopped and not bridged with heparin in our research, regardless of the cause for the interruption. The exact cause for the interruption could not be determined owing to a restriction in the data extraction, but we were able to determine the general pattern. Ischemic events occurred at a rate comparable to that seen in the BRIDGE trial, which had a rate of 0.3-0.4 percent for arterial thrombotic events during a 30-day period.[14,15] Our findings are consistent with existing recommendations. A stroke or TIA is estimated to be 0.35 percent for every 30 days in patients with atrial fibrillation (AF), according to the 2017 American College of Cardiology guidelines.[16-18] The ACC also recommends that an individual's daily risk of stroke or TIA be calculated by dividing the individual's annual risk of stroke or TIA by 365 days.[18-20] This method, on the other hand, is based on research conducted on individuals who were mainly of moderate risk and were having elective operations.

By giving the actual rate of stroke during hospitalisation, which is greater than what would be anticipated based on the ACC method of estimate; our research contributes to the existing body of knowledge in this area. Although the American College of Cardiology (ACC) recommends that patients at highest risk for thromboembolic events without an excessive risk of bleeding should consider bridging, it acknowledges that the decision on whether or not to bridge patients with atrial fibrillation and a high CHA2DS2VASc score is still up for debate. Some doctors, however, believe that bridging anticoagulation is appropriate for patients who have had a verified recent stroke based on the current evidence. The findings of our research are consistent with the recommendations of the American College of Cardiology. It demonstrates that the risk of acute stroke in low-risk individuals (CHA2DS-2VASc<5) is minimal, and that this group may be safely weaned off anticoagulation without danger. And all of the strokes happened in those who were either moderate or high-risk. In patients at

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intermediate and high risk of stroke, there was no statistically significant difference in the incidence of stroke between the two groups, which is most likely owing to the limited number of occurrences.

Conclusion

According to the findings of the present research, the incidence of ischemic stroke in hospitalised patients with atrial fibrillation (AF) is low during hospitalisation and does not increase substantially with short-term anticoagulant cessation. In hospitalised patients with atrial fibrillation (AF), the CHA2DS2VASc score shows a statistically significant relationship with the incidence of ischemic stroke. In order to establish the impact of anticoagulation interruption duration on the incidence of stroke in the high-risk group, further study is required.

Reference

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991; **22**: 983– 8.
2. Bunch TJ, Crandall BG, Weiss JP, May HT, Bair TL, Osborn JS, et al. Patients treated with catheter ablation for atrial fibrillation have long-term rates of death, stroke, and dementia similar to patients without atrial fibrillation. *J Cardiovasc Electrophysiol*. 2011; **22**: 839– 45.
3. Takigawa M, Takahashi A, Kuwahara T, Takahashi Y, Okubo K, Nakashima E, et al. Late-phase thromboembolism after catheter ablation for paroxysmal atrial fibrillation. *Circ J*. 2014; **78**: 2394– 401.
4. Friberg L, Tabrizi F, Englund A. Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. *Eur Heart J*. 2016; **37**: 2478– 87.
5. Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. *J Arrhythm*. 2017; **33**: 369– 409
6. Walkey AJ, Wiener RS, Ghobrial JM, Curtis LH, Benjamin EJ. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. *JAMA*.2011;306(20):2248-2254.
7. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. *Chest*. 2010; 137(2):263-272.
8. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010;138(5):1093-1100.
9. Zeerleder S, Hack CE,WuilleminWA. Disseminated intravascular coagulation in sepsis.*Chest*. 2005;128(4):2864-2875.
10. Siegal D, Yudin J, Kaatz S, Douketis JD, Lim W, Spy-ropoulos AC. Periprocedural heparin bridging in patientsreceiving vitamin K antagonists: systematic review

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andmeta-analysisofbleedingandthromboembolicrates.Cir-culation. 2012;126(13):1630-1639.

11. DouketisJD,HealeyJS,BrueckmannM,EikelboomJW,Ezekowitz MD, Fraessdorf M, Noack H, et al. Periopera-tive bridging anticoagulation during dabigatran or warfa-rin interruption among patients who had an elective sur-gery or procedure. Substudy of the RE-LY trial. ThrombHaemost.2015;113(3):625-632.
12. Cavallari I, Ruff CT, Nordio F, Deenadayalu N, Shi M,LanzH,RutmanH,etal.Clinicaleventsafterinterruptionofanticoagulationinpatientswithatrialfibrilla-tion: An analysis from the ENGAGE AF-TIMI 48 trial.Int JCardiol. 2018;257:102-107.
13. Holbrook A, Schulman S, Witt DM, Vandvik PO, Fish J,Kovacs MJ, Svensson PJ, et al. Evidence-based manage-ment of anticoagulant therapy: antithrombotic therapyand prevention of thrombosis, 9th ed: American CollegeofChestPhysiciansEvidence-BasedClinicalPracticeGuidelines.Chest.2012;141(2Suppl):e152S-e184S.
14. Essebag V, Proietti R, Birnie DH, Wang J, Douketis J,Coutu B, Parkash R, et al. Short-term dabigatran inter-ruptionbeforecardiacrhythmdeviceimplantation:multi-centre experience from the RE-LY trial. Europace.2017;19(10):1630-1636.
15. Kim TH, Kim JY, Mun HS, Lee HY, Roh YH, Uhm JS,PakHN,etal.Heparinbridginginwarfarinanticoagulationtherapyinitiationcouldincreasebleedinginnon-valvularatrialfibrillationpatients:amulticenterpropensity-matchedanalysis.JThrombHaemost.2015;13(2):182-190.
16. You JJ, Singer DE, Howard PA, Lane DA, Eckman MH,Fang MC, Hylek EM, et al. Antithrombotic therapy foratrial fibrillation: Antithrombotic Therapy and Preven-tion of Thrombosis, 9th ed: American College of ChestPhysicians Evidence-Based Clinical Practice Guidelines.Chest.2012;141(2Suppl):e531S-e575S.
17. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D,CasadeiB,CastellaM,etal.2016ESCGuidelinesforthemanagement of atrial fibrillation developed in collabora-tionwithEACTS.EurHeartJ.2016;37(38):2893-2962.
18. Doherty JU, Gluckman TJ, Hucker WJ, Januzzi JL, Jr.,Ortel TL, Saxonhouse SJ, Spinler SA. 2017 ACC expertconsensus decision pathway for periprocedural manage-ment of anticoagulation in patients with nonvalvular atri-alfibrillation:areportoftheAmericancollegeofcardiol-ogy clinical expert consensus document task force. J AmColl Cardiol. 2017;69(7):871-898
19. SteinbergBA,PetersonED,KimS,ThomasL,GershBJ,Fonarow GC, Kowey PR, et al. Use and outcomes asso-ciated with bridging during anticoagulation interruptionsin patients with atrial fibrillation: findings from the Out-comes Registry for Better Informed Treatment of AtrialFibrillation (ORBIT-AF). Circulation. 2015;131(5):488-494.
20. Krishnamoorthy A, Ortel T. A bridge to nowhere? Benefits and risks for periprocedural anticoagulation in atrialfibrillation. Curr Cardiol Rep. 2016;18(10):101.