

Incidence of atrial fibrillation in patients with cryptogenic stroke



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ABSTRACT

Background: Stroke can cause serious disability and mortality among the worldwide population. Atrial fibrillation (AF) is one of the major risk factors for ischemic stroke and a common cause of cardioembolism in old age. **Aims and Objectives:** The aim of the study was to study the incidence of AF in patients with cryptogenic stroke (CS). **Materials and Methods:** A prospective and observational study on AF and stroke was carried out in the Department of Cardiology/Neurology, in a tertiary care hospital. Data were collected in the form of chief complaints, medical history, clinical examination, and treatment given in the enclosed proforma for 1 year. On follow-up, specified goals including hypertension (HTN) management, lipid management, and diabetes management were done as per current guidelines. **Results:** Out of 100 CS patients, 69 were male and the mean age of the patients in this study was 59 ± 13.37 years. The incidence of AF was 11% at the end of 1 year with male predominance (64%) and a mean age of 62 ± 12.94 years. The mean CHADS2 Score in this study group was 1.40 with a standard deviation of 1.31. Stroke reoccurred in 12% of patients at the end of 1-year follow-up. Patients with recurrent stroke were mostly elderly with a mean age of 70 years ($SD = 9.78$, $P = 0.03$). **Conclusion:** It is found that a longer duration of electrocardiographic monitoring after CS increases the proportion diagnosed with AF and should be done in selected high-risk cases, especially in patients with HTN, dyslipidemia, diabetes mellitus, chronic kidney disease, and high CHADS2 score.

Key words: Atrial fibrillation; Cryptogenic stroke; Hypertension

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INTRODUCTION

The prevention of stroke related to atrial fibrillation (AF) is a global public health priority. Strokes due to AF are common and frequently devastating (70–80% of patients die or become disabled).^{1,2} The trial of ORG 10172 in acute stroke treatment (TOAST) criteria define Cryptogenic stroke (CS) as brain infarction that is not attributable to a definite cardioembolism, large artery atherosclerosis, or small artery disease despite extensive vascular, cardiac, and serologic evaluation.³ AF is one of the major risk factors of ischemic stroke and a common cause of cardio embolism in old age. The diagnosis of AF is clinically important because trials have shown

that anticoagulation reduces the risk of stroke in patients with AF.⁴ Antiplatelet therapy can be used as a standard treatment regimen for the secondary prevention of stroke in the absence of AF (22% reduction in risk, as compared with placebo). However, when AF is present, anticoagulant treatment is strongly recommended over antiplatelet agents (39–63% reduction in the risk of stroke as compared with antiplatelet therapy).⁵ Undiagnosed AF can also be suspected as an etiology for many CSs, but anticoagulation is not recommended unless AF has been documented.⁶

Since patients who have had a stroke due to AF face a high annual risk of stroke recurrence,⁷ strategies to improve

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the detection, and treatment of AF promise to reduce the burden of recurrent strokes. Traditional monitoring techniques may fall into false assumptions in detecting AF since it is having paroxysmal and asymptomatic nature.⁸ Nowadays, detection of AF can be done in a hospital setting using serial electrocardiography (ECG), Holter monitoring, monitoring with the use of external event (or loop recorders), long-term outpatient monitoring, and monitoring using insertable cardiac monitors (ICMs).⁹⁻¹⁴ The current guidelines suggest performing 24 or more hours of ECG monitoring to rule out AF in patients with an ischemic stroke and at the same time, the most effective duration of monitoring has not been determined.¹⁰ Due to asymptomatic and intermittent nature of AF, it is suggested that longer cardiac monitoring among patients with CS would have important therapeutic and clinical implications. The CHADS (congestive heart failure, hypertension, age >75 years, diabetes, and stroke or transient ischemic attack [TIA]) scoring system is a helpful tool to determine treatment for AF in patients prone to stroke.¹¹

Aims and objectives

To study the incidence of atrial fibrillation in patients with cryptogenic stroke.

MATERIALS AND METHODS

Study population

Patients who were 40 years of age or older, patients in sinus rhythm with no history of AF, and had an ischemic stroke or TIA of unknown etiology, diagnosed by a neurologist after a standard workup, including 12-lead ECG, brain magnetic resonance imaging or computed tomography scan, ambulatory ECG monitoring with the use of a Holter or telemetry monitor for a minimum of 24 h, and echocardiography were included in this study. Patients were excluded if they had known etiology, pregnancy within 6 months, patients otherwise not available for follow-up, or patients with a concurrent disease which may affect the clinical outcome, an indication for an implantable cardioverter-defibrillator, cardiac resynchronization therapy or an implantable hemodynamic monitoring system, coronary bypass grafting or myocardial infarction <1 month before the stroke, and life expectancy <1 year. Thus, a total of 100 patients meeting the inclusion and exclusion criteria were included in this study.

Study design

This was a single-center, prospective, and observational study conducted over 1 year in a tertiary care hospital. Data were collected in the form of chief complaints, medical history, clinical examination, and treatment given in the semi-structured proforma for 1 year. On follow-up,

specified goals including hypertension management, lipid management, and diabetes management were done as per current guidelines. On discharge, all enrolled patients were followed with external monitoring (Event Loop Recorder/Patch Holter) for 7 days. The first follow-up was done at 14 days. At the end of the prescribed tenure, the rhythm was analyzed both by computer and manually and a report was generated. Subsequent follow-up was done at 4, 8, and 12 months. Every patient was minimally followed for 1 year.

The associations between various categorical variables were assessed using Chi-square/Fisher's exact test. Quantitative variables were expressed as mean±SD and analyzed using the Unpaired Student's t-test. The statistical analysis was done using Statistical Package for the Social Science (SPSS) version 19.0 software.

RESULTS

Out of 100 CS patients, 69% were males and 31% were females. Seven patients were identified to have AF at the end of 14 days with a mean age of 57±13.98 years. During the study period, the incidence of AF detected was 11% at the end of 1 year with male predominance (64%) and a mean age of 62±12.94 years.

Stroke reoccurred in 12% of patients at the end of 1-year follow-up (Table 1). Three patients, five patients, and three patients were found to have stroke recurrence, respectively, at each follow-up (i.e., at 4 months, 8 months, and 1 year, respectively). Patients with recurrent stroke were mostly elderly with a mean age of 70 years (SD=9.78, P=0.03).

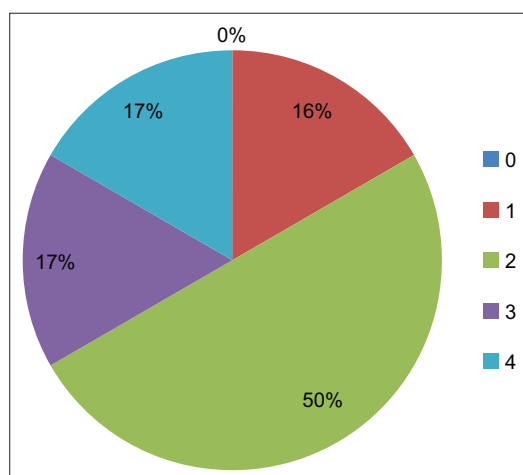
Antiplatelets were used in all patients (100%). However, they were up-titrated to anticoagulants once AF was documented. Antiplatelets along with anticoagulants were continued in patients who had computer-aided design (CAD) along with AF. Statins were given in high doses (80 mg of atorvastatin or 40 mg of rosuvastatin) to 100% of patients as per current guidelines. They were monitored at follow-up for any side effects. The practice of thrombolysis was followed as per current guidelines. Fifteen patients in the study group were thrombolysed as per neurologist discretion.

The mean CHADS2 score in our study group was 1.40 with a standard deviation of 1.31. The Mean CHADS2 score was higher in the AF documented group (mean=2.27, SD=1.009). The CHADS2 score was statistically significant at the end of the study (P=0.02) (Chart 1).

Patients with recurrent stroke had a mean CHADS2 score of 2.33 (SD=0.98, P=0.01).

Table 1: Age and sex distribution among the study group

Age (years)	Total patients			Recurrent stroke patients		
	Female (n=31)	Male (n=69)	Total (n=100)	Female (n=4)	Male (n=8)	Total (n=12)
≤50	9 (9%)	28 (28%)	37 (37%)	0 (0%)	0 (0%)	0 (0%)
51–60	9 (9%)	10 (10%)	19 (19%)	1 (8.3%)	1 (8.3%)	2 (16.6%)
61–70	7 (7%)	12 (12%)	19 (19%)	1 (8.3%)	3 (25%)	4 (33.3%)
71–80	6 (6%)	11 (11%)	17 (17%)	2 (16.6%)	2 (16.6%)	4 (33.2%)
>80	0 (0%)	8 (8%)	8 (8%)	0 (0%)	2 (16.6%)	2 (16.6%)

**Chart 1:** CHADS2 score among recurrent stroke patients

The most observed risk factors for AF were hypertension (51), dyslipidemia (37), diabetes mellitus (DM) (27), and smoking (27), respectively. Other risk factors included a history of stroke, CAD, and chronic kidney disease (CKD).

The incidence of AF was found to be greater in DM and hypertension accounting for nine cases each and six positive cases of AF in dyslipidemia.

Past h/o CAD and HTN was present in 25% and 75% of patients. Statistically significant h/o DM was found in 58% of patients with $P=0.009$. Past h/o CKD ($P=0.414$) and CVA ($P=0.365$) was not found statistically significant (Table 2).

DISCUSSION

AF is an important cause of CS, responsible for between 20% and 58% of all cerebrovascular ischemic events.¹² Systematic reviews assessing the detection of AF with external ECG monitoring in patients after CS have shown a detection rate of newly diagnosed AF of 5–20%.^{6,13}

Data of 100 patients have been taken up for analysis purposes. Heart functions were normal in this study group with a mean EF of 55%. The mean age of patients in our study was 59 ± 13.37 years (69% were males and 31% were females). Thus, males significantly outnumbered

the females in incidence. Out of 100 patients, 7% had documented AF at the end of 14 days.

Higgins et al.,¹⁴ performed a pragmatic randomized trial with objective outcome assessment among patients presenting in sinus rhythm with no AF history, within 7 days of ischemic stroke symptom onset. Patients were randomized to standard practice investigations (SP) to detect AF, or SP plus additional monitoring (SP-AM). AM comprised 7 days of noninvasive cardiac-event monitoring which was to be reported by an accredited cardiac electrocardiology laboratory. One hundred patients were enrolled from two centers. Within 14 days of stroke, sustained paroxysms of AF were detected in 18% of patients undergoing SP-AM versus 2% undergoing SP ($P<0.05$). Although the patient enrolled were not of CS, the investigators concluded non-invasive cardiac-event monitoring should be routinely adopted as the standard of care in all stroke patients who appear to be in sinus rhythm.

In this study, two patients had new AF at first and second follow-up each (i.e., at 4 months and 8 months, respectively). During the study period, the incidence of AF detected was 11% at the end of 1 year with male predominance (64%).

Sanna et al.,¹⁵ showed that among patients with CSs, detection of AF increased further with a longer duration of monitoring up to 3 years. Their controlled study enrolled 441 patients who were randomized in a 1:1 ratio to ICM versus standard arrhythmia monitoring (based on local practice). AF detection rate was 9% at 6 months, 12% at 12 months, and 30% at 3 years in those with CS. The mean age was 62 ± 11.3 years and 64% of patients were males.

Gladstone et al.,¹⁶ aimed at quantifying the benefits of a longer monitoring period for the detecting of paroxysmal AF in the context of secondary stroke prevention for patients deemed to have CSs. They enrolled 572 patients aged ≥ 55 years, without known AF. The 30-day ECG monitoring strategy was superior to 24-h ECG monitoring for the detection of at least one episode of AF. AF lasting 30 s or longer was detected in 45 of 280 patients (16%) in the intervention group, as compared with 9 of 277 (3%) in the control group (absolute difference, 12.9 percentage

Table 2: Characteristics of recurrent stroke patients

Risk Factors	Positive	Male	Female	Negative	P value
Past h/o CAD	3 (25%)	3	0	9	0.301
Diabetes	7 (58.3%)	4	3	5	0.009
Hypertension	9 (75%)	6	3	3	0.076
CVA	4 (33%)	4	0	8	0.365
Smoking	0 (0.0%)	0	0	12	0.025
CKD	1 (8.3%)	1	0	11	0.414
Hyperlipidemia	7 (58.3%)	6	1	5	0.103

points; 95% confidence interval (CI), 8.0–17.6; $P < 0.001$; number needed to screen, 8).

In a study, Choe et al.,¹⁷ propose 12 months of monitoring by implantable loop recorders after ischemic stroke as the gold standard for the detection of post-stroke AF. Using this gold standard, they aimed to estimate the sensitivity of various simulated durations and sequences of Holter monitoring. They estimated that 24-h Holter monitoring had a sensitivity of 1.3%, whereas 30-day monitoring had a sensitivity of 22.8%. Based on these results, the odds of detecting AF with 24-h Holter monitoring, one of the most commonly used diagnostic strategies, is exceptionally low.

In CS patients monitored through external devices, the data have been heterogeneous, AF detection yields have ranged from 3% for 24-h Holter monitors at 90 days in the control arm of the Gladstone et al.,¹⁶ studies to 24% overall in one study using mobile cardiac outpatient telemetry for 28 days.

The overall incidence of HTN and dyslipidemia (DLP) was 51% and 37% in our study group. These two variables represented high-risk groups in our patient population. CS patients with these risk factors should be evaluated beyond the usual 24 h of Holter monitoring for AF.

The mean CHADS₂ score was higher in the AF documented group (mean=2.27; SD=1.009). The CHADS₂ score was statistically significant in our study group ($P=0.02$). Most of the patients in the study by Sanna et al.,¹⁵ had CHADS₂ scores in the range of 2–3 (34% and 41.5%, respectively). The median CHADS₂ score of the patients in a study by Gladstone et al.¹⁶ was 3 points (range, 2–6).

Significant univariate predictors of AF at 12 months in study by Sanna et al.,¹⁵ included age (hazard ratio [HR] per decade 2.0 [95% CI=1.4–2.8], $P=0.002$), CHADS₂ score (HR=1.9 per 1 point [1.3–2.8], $P=0.008$), and diabetes (HR=2.3 [1.0–5.2], $P < 0.05$) among various variables.

Stroke recurrence

The incidence of stroke recurrence was 12% at the end of 1-year follow-up. Patients with recurrent stroke were mostly elderly and had a mean CHADS₂ score of 2.33

($P=0.01$). Statistically significant h/o DM was found in 58% of patients with $P=0.009$.

One patient had paroxysmal AF documented when she had a stroke at external monitoring at follow-up. Stroke reoccurred in one patient who was on anticoagulants as AF was documented at 14 days.

Bang et al.,¹⁸ prospectively studied 204 patients with acute cerebral infarcts to understand the frequency and mechanisms of stroke recurrence after the stroke with no determined cause (NC). Patients of the NC group showed a significantly higher rate (30%) of recurrent stroke than those of other subtypes.

Neither Gladstone et al.,¹⁶ nor the Sanna et al.,¹⁵ evaluated the impact of monitoring strategies on hard clinical outcomes, including recurrent stroke.

In a population-based study in Oxfordshire, UK, among patients with a first TIA or ischemic stroke Li et al.,¹⁹ compared cryptogenic events versus other causative subtypes according to the TOAST classification. Among 2555 patients, 812 (32%) who had cryptogenic events, 9.1% (35) had stroke recurrence at 1 year and 24% (76) at 5 years. 70 (63%) of 112 recurrent strokes after cryptogenic events remained cryptogenic after further investigation.

Arauz et al.,²⁰ analyzed data of consecutive embolic strokes of undetermined source (ESUS) and cardioembolic stroke patients from an institutional database. One hundred and forty-nine ESUS (median age 44 years) and 235 cardioembolic strokes (median age 66 years) consecutive patients were included in the study. The Median follow-up period for the entire sample was 19 months (interquartile range 6.0–45.0 months). Stroke recurrence was similar between ESUS and cardioembolic stroke patients (5.4% vs. 9.8%, respectively, $P=0.12$).

In this study, 83% of recurrent strokes remained cryptogenic at the end of the study. Evaluating patients for AF after a stroke or TIA is important because of the treatment implications. We targeted patients at risk for stroke recurrence who were potential candidates for

anticoagulant therapy, yet in practice, such patients typically receive only antiplatelet therapy if AF is not detected.

When AF is detected, anticoagulation is strongly advised, whether the AF is paroxysmal or sustained because the stroke risks are similar,^{21,22} and patients with either type of AF benefit from anticoagulation.^{21,23,24} We think that the common practice of relying on 24–48 h of monitoring for AF after a CS is insufficient, especially given our finding that the yield of clinical follow-up alone as a means of detecting AF was negligible.

Although our study is one among the few prospective studies for the detection of AF in patients with CS, there were some limitations:

Patients with large and severe strokes, in which cardioembolism is likely to be most prevalent, were underrepresented; however, they were not the target of this trial, which focused on stroke survivors attending outpatient clinics after hospital discharge, most of whom had had mild and non-disabling strokes and were considered to be ideal candidates for secondary stroke prevention. It is unclear whether newly discovered AF was causally related to the index stroke, because not all strokes, even in patients with documented AF, are due to the arrhythmia. Furthermore, we did not study age-matched controls without stroke or TIA.

Limitations of the study

Patients presenting with stroke which is attributable to cardioembolism is likely to be underrepresented; however, they were not the target of this study. It is unclear whether newly discovered atrial fibrillation was causally related to the index stroke because not all strokes, even in patients with documented atrial fibrillation are due to the arrhythmias.

Therefore, a study with a larger sample size and age matched controls without stroke will be resourceful in supporting the findings of this study.

CONCLUSION

A longer duration of electrocardiographic monitoring after CS increases the proportion diagnosed with AF and should be done in selected high-risk cases, especially in patients with HTN, DLP, DM, CKD, and high CHADS2 scores. The future studies are needed to determine the optimal duration of long-term monitoring, which corresponds with the greatest reduction in outcomes, primarily that of recurrent stroke and death.

The incidence of recurrent stroke in our study group was 12% at the end of 1 year. Moreover, prolonged monitoring

increased the proportion of patients who subsequently received anticoagulant therapy for secondary prevention of stroke – A finding we interpret as a clinically meaningful change in treatment that has the potential to avert recurrent strokes.

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REFERENCES

- Gladstone DJ, Bui E, Fang J, Laupacis A, Lindsay MP, Tu JV, et al. Potentially preventable strokes in high-risk patients with atrial fibrillation who are not adequately anticoagulated. *Stroke*. 2009;40(1):235-240. <https://doi.org/10.1161/STROKEAHA.108.516344>
- Saposnik G, Gladstone D, Raptis R, Zhou L, Hart RG, Investigators of the registry of the Canadian Stroke Network and Stroke Outcomes Research Canada (SORCan) Working Group. Atrial fibrillation in ischemic stroke: Predicting response to thrombolysis and clinical outcomes. *Stroke*. 2013;44(1):99-104. <https://doi.org/10.1161/STROKEAHA.112.676551>
- Adams HP Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. *Stroke*. 1993;24(1):35-41. <https://doi.org/10.1161/01.str.24.1.35>
- Angelis MV, Stefano VD, Franciotti R, Furia N, Girolamo ED, Onofri M, et al. Cryptogenic stroke and atrial fibrillation in a real world population: The role of insertable cardiac monitors. *Sci Rep*. 2020;10(1):3230. <https://doi.org/10.1038/s41598-020-60180-6>
- Hart RG, Pearce LA and Aguilar MI. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146(12):857-867. <https://doi.org/10.7326/0003-4819-146-12-200706190-00007>
- Seet RC, Friedman PA and Rabinstein AA. Prolonged rhythm monitoring for the detection of occult paroxysmal atrial fibrillation in ischemic stroke of unknown cause. *Circulation*. 2011;124(4):477-486. <https://doi.org/10.1161/CIRCULATIONAHA.111.029801>
- Stroke Risk in Atrial Fibrillation Working Group. Independent predictors of stroke in patients with atrial fibrillation: A systematic review. *Neurology*. 2007;69(6):546-554. <https://doi.org/10.1212/01.wnl.0000267275.68538.8d>
- Ziegler PD, Glotzer TV, Daoud EG, Singer DE, Ezekowitz MD, Hoyt RH, et al. Detection of previously undiagnosed atrial fibrillation in patients with stroke risk factors and usefulness of continuous monitoring in primary stroke prevention. *Am J Cardiol*. 2012;110(9):1309-1314.
- Douen AG, Pageau N and Medic S. Serial electrocardiographic assessments significantly improve detection of atrial fibrillation 2.6-fold in patients with acute stroke. *Stroke*. 2008;39(2):480-482. <https://doi.org/10.1161/STROKEAHA.107.492595>
- Jauch EC, Saver JL, Adams HP Jr., Bruno A, Connors JJ,

- Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American heart association/American stroke association. *Stroke*. 2013;44(3):870-947.
<https://doi.org/10.1161/STR.0b013e318284056a>
11. Cunha JP. What does Chads Score Mean? *Emedicinehealth*; 2020 Nov 6. Available from: https://www.emedicinehealth.com/what_does_chads_score_mean/article_em.htm. [Last accessed on 10 July 2022]
 12. Jickling GC, Stamova B, Ander BP, Zhan X, Liu D, Sison SM, et al. Prediction of cardioembolic, arterial, and lacunar causes of cryptogenic stroke by gene expression and infarct location. *Stroke*. 2012;43(8):2036-2041.
<https://doi.org/10.1161/STROKEAHA.111.648725>
 13. Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack. *Stroke*. 2014;45(2):520-526.
<https://doi.org/10.1161/STROKEAHA.113.003433>
 14. Higgins P, MacFarlane PW, Dawson J, McInnes GT, Langhorne P and Lees KR. Noninvasive cardiac event monitoring to detect atrial fibrillation after ischemic stroke: A randomized, controlled trial. *Stroke*. 2013;44(9):2525-2531.
<https://doi.org/10.1161/STROKEAHA.113.001927>
 15. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med*. 2014;370(26):2478-2486.
<https://doi.org/10.1056/NEJMoa1313600>
 16. Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, et al. Atrial fibrillation in patients with cryptogenic stroke. *N Engl J Med*. 2014;370(26):2467-2477.
<https://doi.org/10.1056/NEJMoa1311376>
 17. Choe WC, Passman RS, Brachmann J, Morillo CA, Sanna T, Bernstein RA, et al. A comparison of atrial fibrillation monitoring strategies after cryptogenic stroke (from the cryptogenic stroke and underlying AF trial). *Am J Cardiol*. 2015;116(6):889-893.
<https://doi.org/10.1016/j.amjcard.2015.06.012>
 18. Bang OY, Lee PH, Joo SY, Lee JS, Joo IS and Huh K. Frequency and mechanisms of stroke recurrence after cryptogenic stroke. *Ann Neurol*. 2003;54(2):227-234.
<https://doi.org/10.1002/ana.10644>
 19. Li L, Yiin GS, Geraghty OC, Schulz UG, Kuker W, Mehta Z, et al. Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: A population-based study. *Lancet Neurol*. 2015;14(9):903-913.
[https://doi.org/10.1016/S1474-4422\(15\)00132-5](https://doi.org/10.1016/S1474-4422(15)00132-5)
 20. Arauz A, Morelos E, Colín J, Roldán J and Barboza MA. Comparison of functional outcome and stroke recurrence in patients with embolic stroke of undetermined source (ESUS) vs. cardioembolic stroke patients. *PLoS One*. 2016;11(11):e0166091.
<https://doi.org/10.1371/journal.pone.0166091>
 21. Hohnloser SH, Pajitnev D, Pogue J, Healey JS, Pfeffer MA, Yusuf S, et al. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: An ACTIVE W substudy. *J Am Coll Cardiol*. 2007;50(22):2156-2161.
<https://doi.org/10.1016/j.jacc.2007.07.076>
 22. Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL, et al. Stroke with intermittent atrial fibrillation: Incidence and predictors during aspirin therapy. *J Am Coll Cardiol*. 2000;35(1):183-187.
[https://doi.org/10.1016/s0735-1097\(99\)00489-1](https://doi.org/10.1016/s0735-1097(99)00489-1)
 23. Al-Khatib SM, Thomas L, Wallentin L, Lopes RD, Gersh B, Garcia D, et al. Outcomes of apixaban vs. Warfarin by type and duration of atrial fibrillation: Results from the ARISTOTLE trial. *Eur Heart J*. 2013;34(31):2464-2471.
<https://doi.org/10.1093/eurheartj/eh135>
 24. Flaker G, Ezekowitz M, Yusuf S, Wallentin L, Noack H, Brueckmann M, et al. Efficacy and safety of dabigatran compared to warfarin in patients with paroxysmal, persistent, and permanent atrial fibrillation: Results from the RE-LY (Randomized evaluation of long-term anticoagulation therapy) study. *J Am Coll Cardiol*. 2012;59(9):854-855.
<https://doi.org/10.1016/j.jacc.2011.10.896>

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AS- Concept and design of the study, prepared first draft of manuscript, interpreted the results; reviewed the literature and manuscript preparation, concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript; **AB-** Concept and design of the study, prepared first draft of manuscript, interpreted the results; reviewed the literature, and manuscript preparation; **RPS-** Interpreted the results; reviewed the literature and manuscript preparation, concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript; **AKP-** Concept and design of the study and prepared first draft of manuscript; **RG-** Concept and design of the study and prepared first draft of manuscript; and **SVM-** concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript.

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