

Original research article

Anticoagulation Therapy for Non-Valvular Atrial Fibrillation

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Abstract

Background: Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia accounting for one-third of all arrhythmia related hospitalizations. AF is major risk factor for stroke. Atrial fibrillation is hyper coagulable state in both paroxysmal and chronic atrial fibrillation, AF related stroke can be effectively prevented with oral anticoagulant therapy with vitamin K antagonist or non vitamin K antagonist. The present study was done with objective to detect prevalence of use of anti coagulants in treatment of non-valvular atrial fibrillation.

Methods: This was a descriptive cross-sectional observational type of study done at Narayan medical college and hospital Jamuhar, Sasaram, department of Medicine on 200 patients of non-valvular atrial fibrillation. Non-valvular atrial fibrillation patients were defined as atrial fibrillation without rheumatic valvular disease predominantly mitral stenosis or mechanical heart valves. Data regarding patients' demographics, co-morbidities, diagnosis of AF were recorded; CHA2DS2_Vasc and HASBLED scores were calculated for each patient.

Results: In this study out of total 200 study subjects, 50 study subjects had CHA2DS2_Vasc score less than 1, whereas 150 study subjects have score more than 1. Out of 150 eligible patients only 15 were on anticoagulants.

Conclusions: In this study, it was found that the majority of patients with non-valvular AF were not anti-coagulated (90%), the type of anticoagulant most commonly used was vit K antagonist and most common risk factors for bleeding are hypertension (72%) followed by heart failure (36%).

Introduction

Atrial fibrillation (AF) is the most prevalent persistent cardiac dysrhythmia in the world, with an increasing frequency. In addition to producing severe symptom load, AF is a major cause of morbidity and mortality due to the risk of stroke that comes with it. Cardio-embolism appears to be a prominent contributor in AF-related stroke, despite the fact that the complete causal pathways are still being investigated. ⁽¹⁾ Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia, accounting for one-third of all arrhythmia-related hospitalizations. AF now affects 2.5 million persons in the United States; but, because to the ageing "baby-boomer"

population, this number is predicted to rise to an estimated 16 million by 2050. 2 Ischemic stroke is one of the most worrying complications of AF, with an annual incidence of roughly 5% in the absence of effective prevention. (2) Different types of AF: Paroxysmal AF with a high arrhythmia load has a stroke risk that is equivalent to chronic or persistent AF. There are two types of AF: valvular and non-valvular. AF that isn't caused by a mechanical heart valve or moderate-to-severe mitral stenosis is known as non-valvular AF. (3)

Chronic non-valvular atrial fibrillation is associated with a 4.5 percent annual risk of thromboembolic consequences. Age, previous stroke or acute cerebral ischaemia, diabetes, hypertension, and left ventricular dysfunction are all known risk factors. Oral anticoagulant therapy with warfarin has been shown in placebo-controlled trials to be efficacious for primary and secondary prevention of ischemic stroke, reducing the risk by 68 percent. (4)

Stroke is caused by a variety of pathophysiological pathways in patients with atrial fibrillation. Stasis in the left atrium and left atrial appendage, which leads to thrombus development, is widely acknowledged as a key cause of systemic thromboembolism. Stretch-induced processes and endothelial dysfunction may lead to a prothrombotic condition and endothelial dysfunction as a result of left atrial volume overload and dilation. In addition, the beginning of atrial fibrillation may cause hemostatic factors to become activated. Atrial fibrillation has been linked to a hypercoagulable state in both paroxysmal and chronic atrial fibrillation, according to several investigations. Furthermore, increased plasma concentrations of platelet activation markers (beta thromboglobulin, platelet factor IV, and soluble P-selection), thrombogenesis markers (thrombin–antithrombin complexes), and evidence of endothelial dysfunction and damage (von Willebrand factor) have been shown to be independent correlates of thromboembolism. (5)

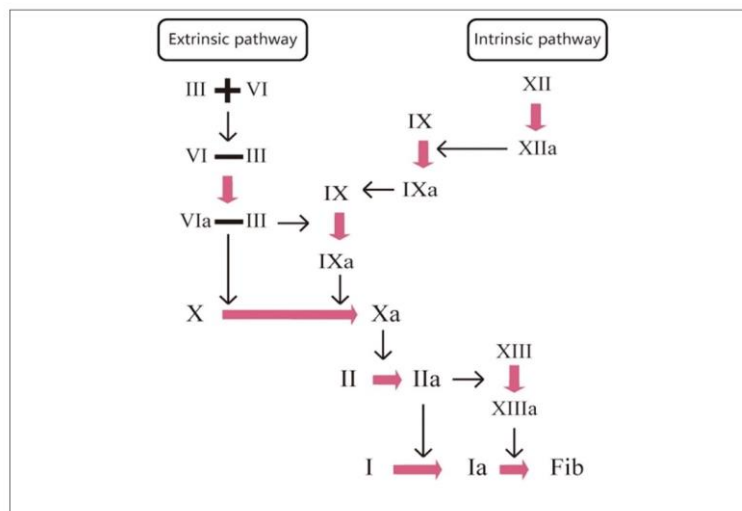


Figure 1 | Anticoagulant Action Mechanism (6)

AF-related strokes are more often fatal or associated with greater permanent neurological deficit than strokes from other causes, but they can be effectively prevented with oral anticoagulant therapy (OAC) with well-controlled vitamin K antagonists (VKAs) or non-vitamin K antagonist oral anticoagulants (NOACs), such as apixaban, rivaroxaban, dabigatran, or endoxaban. (7)

Since its debut in the 1950s, anticoagulation with vitamin K antagonists (VKA) has been the gold standard for stroke prevention in AF, as well as the prophylactic and long-term therapy of venous thromboembolism. By blocking vitamin K-dependent γ -carboxylation, VKAs like phenprocoumon and warfarin impede hepatic synthesis of coagulation components II, VII, IX, and X. VKA treatment necessitates more or less frequent monitoring of the anticoagulant effect with dose adjustment because to the wide range of food and drug interactions, many clinical states, and the unpredictability of genetically determined interindividual variances in drug metabolism. ⁽⁸⁾

TTR is the gold standard for determining the long-term effectiveness of anticoagulation therapy and the risk–benefit profile of warfarin. TTR is the percentage of time that a patient's INR levels are between 2 and 3, with a TTR of 60 percent to 70 percent or greater providing the most benefit. ⁽⁹⁾

AIM OF THE STUDY

To study the prevalence of use of anticoagulants in the treatment of non-valvular atrial fibrillation

MATERIAL AND METHODS

This study is a descriptive observational type of study done at Narayan medical college Jamuhar, Sasaram, Department of Medicine during May 2020 to May 2021 on 200 patients of non-valvular atrial fibrillation.

INCLUSION CRITERIA

All willing patients over 18 years of age, of both sexes with a diagnosis of AF of non-valvular (NVAf) aetiology

EXCLUSION CRITERIA

Patients with a diagnosis of AF with incomplete records were excluded
Those not willing to give consent.

METHODOLOGY

Cross-sectional observational study based on patients with non-valvular AF who will be hospitalized in department of medicine or visiting in Medical OPD at a tertiary hospital during a period of six consecutive months. Non-valvular AF patient was defined as AF patient without rheumatic valvular disease predominantly mitral stenosis or mechanical heart valves. Data regarding patients' demographics (age and gender); comorbidities (ischemic heart disease, congestive heart disease, peripheral vascular disease, diabetes mellitus, hypertension, hyperthyroidism, chronic lung disease, chronic kidney disease, past or active malignancies); diagnosis of AF (new or pre-existing) will be recorded ; CHA2DS2_Vasc and HASBLED scores will be calculated for each patient. Their records will be analysed for use of Anti coagulants (AC) or Anti platelets (AP) drugs. If they are found to be on AC or AP , there INR will be analysed from previous report to know about TTR. For ease of simplicity we will use traditional method for TTR calculation. The traditional method calculates TTR as **the proportion of in-range INR values to the total number of INR values.**

Calculation of CHA2DS2_Vasc Score (Craig T. January et al 2019)¹⁸

1 point	Congestive heart failure
1 point	Hypertension

2 points	Age \geq 75 years
1 point	Diabetes mellitus
2 points	Stroke/Transient Ischemic Attack/Thromboembolic event
1 point	Vascular disease (prior MI, PAD, or aortic plaque)
1 point	Age 65 to 74 years
1 point	Sex category (ie, female sex)

Calculation of HASBLED Score (Lip GY et al ,2011)¹⁹

Letter	Clinical characteristic*	Points
H	Hypertension (i.e. uncontrolled blood pressure)	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding tendency or predisposition	1
L	Labile INRs (for patients taking warfarin)	1
E	Elderly (age greater than 65 years)	1
D	Drugs (concomitant aspirin or NSAIDs) or excess alcohol use (1 point each)	1 or 2

Statistical analysis

Continuous variables were expressed as mean, while categorical data were summarized as frequencies and percentages of patients. The predictors for prescribing NOACs during hospitalization were developed by univariate analysis. All P-values were two-sided, a P values All willing patients over 18 years of age, of both sexes with a diagnosis of AF of non-valvular (NVAf) aetiology.

RESULTS

In this study out of total 200 study subjects, 50 study subjects had CHA₂DS₂-VASc score less than 1, whereas 150 study subjects had score more than 1.

Table 1: CHA₂DS₂-VASc scald score in patients with nonvalvular fibrillation.

CHA ₂ DS ₂ -VASc score	n (%)	Non-anticoagulated n (%)	Anticoagulated, n (%)	p
6	16 (11)	12 (8.89)	4 (26.67)	0.705
4	39 (26)	31 (22.96)	8 (53.33)	0.151
3	87 (58)	84 (62.22)	3 (20)	<0.001
2	8 (5)	8 (5.93)	0	0.001
Total	150	135	15	

CHA₂DS₂-VASc: stroke risk assessment scale.

Regarding the score obtained on the CHA₂DS₂-VASc scale in patients with NVAf, the maximum score achieved was 6 points in 16 (11%) patients and the most frequent score was 3 obtained in 87 (58%). In non-anticoagulated group 12(8.89%) subjects had CHA₂DS₂VASc score 6, whereas its in 4(26.67%) subjects in anticoagulated study subjects. Maximum 84(62.22%) subjects in non-anticoagulated group had score 3 whereas 3(20%) subjects in anticoagulated group had score 3.

Table 2: Distribution of patients with nonvalvular atrial fibrillation according to risk factors used in the CHA₂DS₂-VASc scale.

Risk factors	n = 150 (%)	Not Anticoagulated n = 135 (%)	Anticoagulated n = 15 (%)	p

Heart failure	54 (36.0)	50 (37.03)	4 (2.66)	<0.001
HTN	108 (72.0)	98 (72.59)	10 (66.67)	<0.001
Age > 75 years	63 (42)	48 (35.55)	15 (100)	0.850
Diabetes mellitus	22 (14.66)	14 (10.37)	8 (53.33)	0.064
ACV / AIT	22 (14.66)	8 (5.93)	14(93.33)	0.064
Age between 65-74 years	85 (56.67)	85 (62.96)	0	<0.001

Out of 150 eligible patient only 15 were on anticoagulants. Patients who received dual antiplatelet agents obtained an average of 4.2 points on the CHA₂DS₂-VASc scale. In patients who received anticoagulation, the average of points on the CHA₂DS₂-VASc scale was 3.5 points. Those who hadn't received anticoagulation the most common risk factors were hypertension 108 (72%), age between 65-74 years 85 (56.67%) and heart failure 54 (36%), whereas the group of anticoagulated patients the risk factors for HTN was in 10(66.67%), heart failure in 4(26.67%), age >75yrs in 15(100%) and diabetes mellitus in 8(53.33%).

Table 3: Distribution of patients with nonvalvular atrial fibrillation according to risk factors used in the HAS-BLED scale.

Risk factors	n = 150 (%)	Non -Anticoagulated n = 135 (%)	Anticoagulated n = 15 (%)	p
HTN	108 (72)	93 (68.89)	15 (100)	<0.001
Age > 65 years	148 (98.66)	133 (98.52)	15 (100)	<0.001
Previous stroke	21 (15.7)	10 (7.41)	11 (73.33)	0.064

In patients who received anticoagulation, on the HAS-BLED scale, the average of points obtained was 1.9 and the most common risk factors were hypertension in 108 (72%) patients, age over 65 years in 148 (98.66%) patients. In non anticoagulated group 133(98.52%) subjects had age >65 years, whereas 93(68.89%) subjects had hypertension. In Anticoagulated group 15(100%) had HTN and 15(100%) also had age>65 years.

DISCUSSION

In this study, it was found that the majority of patients with NVAf were not anticoagulated (90%), the type of anticoagulant most used was VKA, and the most common risk factors for bleeding were Hypertension (72%) followed by heart failure (36%). These findings are in accordance to study by **Masahiro Yasaka** et al (2021)(10) where hypertension(85%) was the most common risk factor followed by cerebrovascular disorders(69.5%). Hypertension was the most prevalent comorbidity (38.5%), followed by heart failure (19.8%), prior stroke (13.7%) and diabetes (13.6%) in a study by **Pedro Gabriel Melo de Barros e Silva** et al (2019)(9) Most patients reported in the present study (57.8%) were between the age 65-74 years followed by 42.1% patients above 75 years. In a study by **Jason Shafarin** et al (2016)(11) maximum patients(33.5%) were in the age group 75-84 years. Maximum patients were of the age 81.4 ±4.8 years in study by **Masahiro Yasaka** et al (2021)(10). In a study by **Pedro Gabriel Melo de Barros e Silva** et al (2019)(9) mean age was 63.9 ± 14.7 years and 50.7% were females. In the present study CHA₂DS₂-VASc scale in patients with NVAf, the maximum score achieved was 6 points in 16 (11%) patients and the most frequent score was 3 obtained in 87

(58%). In a study by **AVERROES** et al(2011)(12) mean CHADS₂ was 2.0, similar findings in study by **ARISTOTLE** et al(2011)(13) where it was 2.1. In a study by **Jason Shafrin** et al (2016)(11) mean CHA₂DS₂-VASc score was 3.2. In a study by **Pedro Gabriel Melo de Barros e Silva** et al (2019)(9) mean CHA₂DS₂-VASc score was 2.45 ± 0.88.

In the present study HAS-BLED scale, the average of points obtained was 1.9 and the most common risk factors were hypertension in 108 (72%) patients, age over 65 years in 148 (98.6%) patients. In a study by **Ken Okumura** et al (2020)(14) HAS-BLED score was >3 in 21.1% of total 32,726 patients. In a study by **Jason Shafrin** et al (2016)(11) mean HAS-BLED score was 2.7. In a study by **Masahiro Yasaka** et al (2021)(10) 25810 patients had HAS-BLED score ≥ 2, 6916 had ≥ 3.

So we see that the most of the patient are not on anticoagulation in spite of needing one .This increases the chances of stroke in these patients . all the major guidelines advocate use of anticoagulants in NVAf but still its far from reality in ground level in rural population. Almost same findings were found by different authors. **Pharithi RB et al** ⁽¹⁵⁾ in 2019 conducted a study in which 348 patients AF and increased risk of stroke (CHA₂DS₂-VASc score > 1 for men and > 2 for women) were studied. Forty-eight percent were female with a mean age 71 ± 18.6 years, 52% of whom were > 75. Mean CHA₂DS₂-Vasc and HAS-BLED scores were 4.1 ± 1.8 and 1.4 ± 0.8, respectively. Rivaroxaban, dabigatran and apixaban were prescribed to 154 (54.2%), 106 (34.3%) and 41 (13.2%) patients, respectively. 20.4% had inaccurate prescriptions; 92.9% (n = 65) underdosed and 7.1% (n = 5) on inappropriately higher doses. **Bartholomay E et al** ⁽¹⁶⁾ in 2014 conducted a study in Brazil which found that only 37.6% of patients classified as high risk according to the CHADS₂ scores and 35.5% according to the CHA₂DS₂VASc used oral anticoagulation. **Chebrolu P et al** ⁽¹⁷⁾ published a study in 2020 titled Quality of anticoagulation with warfarin in rural Chhattisgarh stated that “INR values were subtherapeutic two-thirds of the time, and TTR values were poor regardless of distance from the health centre. Future studies should be done to identify interventions to improve INR control”.

Conclusion:

In spite of all guideline advocating use of anti-coagulants as per CHA₂DS₂-VASc score and bleeding risk (HAS-BLED) , very few of NVAf patients in rural india are being put on anticoagulants. Number of cardiologists is very low in this set up, so more focus should be put on family physicians of these areas to evaluate and prescribe required drugs in these patients.

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