

Antithrombotic Adherence to guideline-directed therapy and risk profile among Non-Valvular Atrial fibrillation patients

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Abstract

Introduction: Patients with Atrial fibrillation (AF) are at fivefold higher risk for Ischemic stroke than in the general population. Although the current therapeutic guidelines recommend the use of anticoagulants for thromboembolic prophylaxis in patients with nonvalvular AF (NVAf) with additional risk factor(s) for stroke, the global registry data show non-adherence to guidelines for the management of stroke in different regions of the world. The current study conducted at the tertiary referral cardiac center of Nepal for addressing the risk profile of stroke based on the current risk scores and the use of antithrombotic agents NVAf patients.

Methodology: This was a descriptive observational cross sectional study conducted at Shahid Gangalal National Heart Centre (SGNHC), Kathmandu, Nepal from December 2020 to June 2020 which included patients with Nonvalvular AF. The main objective of the study was to study the clinical characteristics, stroke risk profile based on CHA₂DS₂-VaSc score and risk of bleeding based on HAS-BLED score and the patterns of use of antithrombotic agents in NVAf patients.

Results: A total of 79 cases of NVAf were included with 48(60.8%) males and 31(39.2%) females. The mean CHA₂DS₂-VaSc and HAS-BLED score were 2.44±1.2 and 1.51±1.4 respectively. The majority patients 38% had permanent AF followed by 25.5% had paroxysmal AF. Majority of patients were symptomatic with 67.1% presented with palpitation while 32.9% presented with shortness of breath (SOB). Based on the European Heart Rhythm Association (EHRA) AF related symptoms score, 41.8% had EHRA 2a and 2b while 1.3% had EHRA 4 score. The use of anticoagulants in patients with Nonvalvular AF was 41.6%, with NOACS in 33 % and warfarin used in 8.9 % cases. The majority of patients 51.8% of study population were using anti-platelet agents with aspirin in 49.3 % and clopidogrel in 2.5 % cases while no medication in 6.3 % of cases. Although 70.8 % patients had CHA₂DS₂-VaSc score of 2 or more but the use of anticoagulants was only 58.9 % with 46.4% NOACS and 12.5 % using warfarin among this group of patients.

Conclusion: Although the use of anticoagulant with NOACS in patients with higher risk of stroke is increasing, it is still underused in the majority of cases. There is a need of nationwide AF registry and the need of adoption of the current recommended guidelines to increase use of Anticoagulants in patients with Nonvalvular AF patients for the prevention of stroke.

Keywords: Antithrombotic agents, Nonvalvular AF, Risk profile

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Introduction

Atrial fibrillation (AF) is one of the most common forms of arrhythmias encountered in clinical practice with a global burden of 46.3 million in 2016 and projected to rise above 72 million in Asia alone by the year 2050.^{1,2}

Patients with AF are at greater risk of arterial thromboembolism, amongst which ischemic stroke is the most predominant with a fivefold higher risk than in the general population.^{3,4} The risk increases even

further with the concurrent presence of specific stroke risk factors/modifiers. The current therapeutic guidelines recommend the use of anticoagulants for thromboembolic prophylaxis in patients with nonvalvular AF (NVAf) with additional risk factor(s) for stroke.⁵ However, global registry data show non-adherence to guidelines for the management of stroke in different regions of the world.⁶ The scenario in Nepal has been depicted by two studies conducted by Dhungana et al assessing the risk profile and the need for oral

anticoagulants with risk predicting CHADS2 score > 2.^{7,8} These two studies showed that among patients with NVAF only 18.9 % and 25.3% of patients were using anticoagulant (warfarin) respectively. The studies focusing only with patients with Nonvalvular patients and with the availability of newer anticoagulants is lacking in our part of the world. So, the current study was conducted at the tertiary referral cardiac center of Nepal to address the clinical characteristics, stroke risk profile based on CHA₂DS₂-VaSc score and risk of bleeding based on HAS-BLED score and the patterns of use of Antithrombotic agents in NVAF patients..

Method

This is a descriptive observational cross-sectional study conducted at Shahid Gangalal National Heart Centre (SGNHC), Kathmandu, Nepal from December 2020 to June 2020 among Nonvalvular AF patients. The Ethical approval was taken Institutional review board of SGNHC. We included patients aged >18 years attending SGNHC and diagnosed with Nonvalvular AF and providing consent. Patients diagnosed with valvular AF and not willing to provide consent were excluded. Consecutive sampling was done and the sample size was calculated using the based on prevalence of on nonvalvular AF with estimated prevalence 25.3%⁷ and margin of error(10%). Data were entered into an electronic spreadsheet (Microsoft Excel, Redmond) and the statistical analysis was done using Statistical Package of Social Science (SPSS) version 20. All parametric data were expressed as mean and standard deviation (SD) & nonparametric values were expressed in number and percentage(%).

Pre-tested questionnaires and hospital records were used to collect data which included age, gender, heart rate, basal metabolic index (BMI), duration of AF diagnosis, type of AF, symptoms, European Heart Rhythm Association (EHRA) AF-related symptoms scale, and risk factors (history of diabetes, hypertension, congestive heart failure, previous history of ischemic stroke, peripheral vascular disease, etc) and risk of stroke based on CHA₂DS₂-VaSc score and risk of bleeding based on HAS-BLED score. Data regarding treatment regimens including the use and disuse of antithrombotic medication were also recorded. Cases of AF were diagnosed based on the presence of any of the following electrocardiographic findings: a. Irregularly irregular R-R intervals (when atrioventricular conduction is not impaired), b. absence of distinct repeating P waves, and c. irregular atrial activations. The further distinction to Nonvalvular AF was based on the 2014 American Heart Association (AHA) guidelines which define Nonvalvular AF as that "in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair."⁵ were included in the study.

Results

A total of 79 cases of NVAF were included with 48(60.8%) males and 31(39.2%) females. The mean heart rate was 89.7± 24.34. The mean BMI (kg/m²) was 22.5±2.9. The mean CHA₂DS₂-VaSc and HAS-BLED score were 2.44±1.2 and 1.51±1.4 respectively. On classifying the type of AF; we found that the majority comprising 30(37.99%) had permanent AF followed by 20(25.31%) had paroxysmal AF (Table 1). Majority of patients in study population were symptomatic with, 53(67.09%) presented with palpitation while 26(32.91%) presented with shortness of breath (SOB). AF-related symptoms were classified using European Heart Rhythm Association (EHRA) score; which showed 33 (41.78%) had EHRA 2a and 2b while only 1(1.26%) had EHRA 4. (Table 2)

The stroke risk stratification was done using the CHA₂DS₂-VaSc score; where 1(1.26 %) had a score of 0, 22(27.85%) had a score of 1 while majority of patients had 56(70.89%) had a score 2 or

more with 5(6.32%) having the maximum score 5. The majority 42 (53.17%) had HAS-BLED score of 1 followed by 32(40.52%) who had a score of 2 in Table 3.

The use of anticoagulants in patients with Nonvalvular AF was 41.78% (33) with NOACS in 32.92 % (26) and warfarin used in 8.86 % (7) cases. The majority of patients 51.91% (41) of study population were using antiplatelet aspirin in 49.38 % and clopidogrel in 2.53 % cases while no medication was used in 6.32 % of cases (Table 4).

Although 70.89 % patients had CHA₂DS₂-VaSc score of 2 or more but the use of anticoagulants was only 58.92 % with 46.42% NOACS and 12.50 % using warfarin among this group of patients (Table 5).

Table 1. Baseline Clinical characteristics of the study population (n=79)

Age in years (mean±SD)	65± 10.5
Gender	
Male (n/%)	48(60.75%)
Female (n/%)	31(39.25%)
Heart Rate (mean±SD)	89.7±24.34
Body mass index (mean±SD)	22.5±2.9
Time in months after diagnosis of AF (median, IQR)	12 (6,12,51)
CHAD ₂ DS ₂ VaSc score (mean±SD)	2.44±1.2
HASBLEED score (mean±SD)	1.51±1.4
Type of AF	n/%
First episode	7(8.86%)
Paroxysmal	20(25.31%)
Persistent	13(16.45%)
Longstanding persistent	9(11.39%)
Permanent	30(37.99%)

Table 2: Symptoms and EHRA symptoms scale of study population

Parameter	n/%
Symptoms	
Palpitations	53(67.09%)
SOB	26(32.91%)
EHRA symptoms scale	
1	9(11.39%)
2a	33(41.78%)
2b	33(41.78%)
3	3(3.79%)
4	1(1.26%)

Table 3. CHA₂DS₂VaSc and HAS-BLED score among the study population

CHA ₂ DS ₂ VaSc Score	n/%
0	1(1.26%)
1	22(27.85%)
2	18(22.79%)
3	22(27.85%)
4	11(13.93%)
5	5(6.32%)
HAS-BLED SCORE	n/%
0	1 (1.26%)
1	42 (53.17%)
2	32(40.52%)
3	3(3.79%)
4	1(1.26%)

Table 4. Antiplatelet and anticoagulation use in Nonvalvular AF patients

Medication	n/%
Antiplatelets	
Aspirin	39(49.38%)
Clopidogrel	2(2.53%)
Anticoagulants	
Warfarin	7(8.86%)
Rivaroxaban	13(16.46%)
Dabigatran	13(16.46%)
None	5 (6.32%)

Table 5: Use of anticoagulants in patients with CHA₂DS₂-VaSc ≥ 2 (n=56)

Medication	n/%
Anticoagulants use	33(58.92 %)
Warfarin	7(12.50%)
NOACS:	
Rivaroxaban	13(23.21%)
Dabigatran	13(23.21%)

Discussion

In our study mean age of the patients were 65 ± 10 years of age with male patients predominance which were similar to study done in other parts of world by C. Narasimhan et al in realize AF survey done india, nationwide study done by R. Krittayaphong et al in Thailand , Y. Sun et al in CRAf registry from china , reports from euro heart survey by R. Nieuwlaat et also.⁹⁻¹² Our study shows male preponderance of 60.75% as compared to other various study done in our country which showed female preponderance as the studies have included both valvular and nonvalvular AF and as in our country as Rheumatic heart disease involving mitral valve is the most common cause of valvular AF and the common in female patients.¹³⁻¹⁷

The mean CHA₂DS₂-VaSc and HAS-BLED score were 2.44±1.2 and 1.51±1.4 , respectively showing higher risk of stroke in the study

population which were which were similar to other various study Kerala AF registry , Multicenter study in Thailand ,report from the euro heart survey on AF.^{10,12,18}

The type of atrial fibrillation in ours study as in order with 37.99% had permanent AF followed by 25.31% had paroxysmal AF, 16.45 % had persistent AF, Long standing persistent in 11.39% and first episode in 8.86 % similar to the various other study where permanent AF followed by paroxysmal AF and persistent AF accounts for majority of the type of AF.^{9,10,12,18}

Assessing the AF-related symptoms based on European Heart Rhythm Association (EHRA) score majority of patients in our study (88.61%) were symptomatic with complains palpitations (67.09%), Shortness of Breath (32.91%) with EHRA symptom scale ≥ 2 which was similar to a community-based study that majority of AF patients were symptomatic (EHRA >2) and had impaired quality of life . AF symptoms and lower quality of life are associated with higher risk of hospitalization.¹⁹

Although majority of patients had high risk of stroke 70.89 % with CHA₂DS₂VaSc-score of ≥ 2 only 58.92 % were taking anticoagulant with 46.42% NOACS and 12.5 % using warfarin among this group of patients. Various registries done in Western population such as the ORBIT AF registry and EORP AF conducted in European countries studies confirmed a high rate of anticoagulant use (76% and 80%, respectively) in patients with higher risk of stroke with CHA₂DS₂VaSc-score of ≥ 2.^{20,21} The use of oral anticoagulant in AF patients differs between western and the Asian countries wherewith difference in the rate of anticoagulant use (90% vs. 52%) and NOAC use (52% vs. 28%) as shown in GLORIA phase 2 study.²² Ours study showed similar trends of underuse of oral anticoagulant in our part of the world in indicated patients. However, the use of anticoagulant in patients with Non Valvular AF with higher risk of stroke has been increased compared to previous study article published from Nepal where the use of oral anticoagulant (esp. only with warfarin) varied from 9.6 % to 25.3 %.^{7,8,16,17} The reason behind the increasing use of oral anticoagulant with NOACS is that with the increase availability of Novel anticoagulants such as rivaroxaban and dabigatran as national level pharmaceutical company produces it in recent years and as this study was done in tertiary cardiac center patients whom were mostly managed by cardiologist with adoption of the current recommended guidelines.

Although this study has some limitation is that it is single center descriptive study with less sample size, this is the study done in our part of the world after the availability of NOACs in our country showing that the use of NOACs in our country is increasing trends with the availability of the drugs. A need of national registry involving multicenter study will reflect the true picture on clinical profile and anticoagulant use in patients with nonvalvular AF Patients in our country.

Conclusion

The majority of patients with Nonvalvur AF were symptomatic and has higher risk of stroke based on CHA₂DS₂VaSc-score. The use of anticoagulant with NOACS in patients with higher risk of stroke is increasing, however in the majority of cases, it is still underused. A need of nationwide AF registry is needed to reflect the true picture on the current trends on management of AF in our country. The adoption of the current recommended guidelines is needed to increase use of Anticoagulants in patients with Nonvalvular AF patients in indicated patients.

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