

RISK OF THROMBOEMBOLISM IN NON-VALVULAR ATRIAL FIBRILLATION AND ADEQUACY OF ANTICOAGULATION IN HIGH RISK PATIENTS

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Date Received: June 02, 2018

Date Revised: Aug 17, 2018

Date Accepted: Sep 16, 2018

Contribution

FF conceived, designed and wrote manuscript. MH and MRK did data collection. MK did review and final approval of manuscript. All authors contributed equally.

All authors declare no conflict of interest.

This Article May Be Cited As: Farooq F, Hashim M, Khalid MR, Karim M. Risk of thromboembolism in non-valvular atrial fibrillation and adequacy of anticoagulation in high risk patients. Pak Heart J 2018; 51 (04):314-8

ABSTRACT

Objective: To assess frequency of non-valvular AF, with high risk of thromboembolism and their adequacy of anticoagulation.

Methodology: This study was conducted at National Institute of Cardiovascular Disease Karachi from 1st May to 30th September 2017, included patients with non-valvular AF. Patients were stratified according to thromboembolic risk on CHA₂DS₂-VASc score with more than or equal to 2 as high risk. Information about different types of anticoagulant medications was obtained along with recent INR level. SPSS 19 was used for the analysis of data and t-test, and Chi-square tests were applied for the assessment and comparison of data. Two sided $p \leq 0.05$ was taken as criteria for statistical significance.

Results: A total of 160 patient were studied, 52.5% (84) were males, 85.6% (137) found to have CHA₂DS₂-VASc score 2 or above. Out of them 62.8% (86) were taking warfarin and 13.1% (18) were taking Novel oral anticoagulant (NOAC). Out of those at high risk on warfarin only 20.9% (18), were adequately anticoagulated.

Conclusion: In our study majority of patients with non-valvular AF were at higher risk of thromboembolism with inadequate anticoagulation. Strategies to improve anticoagulation are needed in this group.

Key Words: Atrial fibrillation, Anticoagulation, Thromboembolism, Warfarin, Non valvular atrial fibrillation

INTRODUCTION

Atrial fibrillation (AF) is the commonest form of cardiac arrhythmia.¹ Its incidence increases with advancing age, and hypertension.^{2,3} AF is associated with a substantial health-care and economic burden, and is associated with high risk of cardiovascular mortality and morbidity.⁴ It increases the risk of thromboembolic events, such as ischemic stroke, by 3–5-fold.⁵⁻⁷ All the recent guidelines are advocating assessment of thromboembolic risk and appropriate long term anticoagulation in patients with non valvular atrial fibrillation.⁸⁻¹⁰ The CHADS₂ and CHA₂DS₂-VASc scoring systems are the most popular tools to estimate individual stroke risk.¹¹⁻¹³

At present Vitamin K antagonist are widely used effectively to reduce risk of stroke in high risk non valvular AF patients, but because of strict monitoring, interactions with food and drugs and narrow therapeutic index, there is an inhibition in prescribing and difficulties in achieving appropriate anticoagulation in high risk patients, world over.¹⁴⁻¹⁹ One of local study done by Ikramullah et al. only 27.5% of patients with high risk of stroke according to CHA₂DS₂-VASc were treated with oral anticoagulation although they have not mentioned the level of anticoagulation in these treated patients and included two valvular patients as well.²⁰

The aim of this study was to identify the frequency of high risk non valvular AF patients, according to CHA₂DS₂-VASc score and their adequacy of anticoagulation as well.

METHODOLOGY

This cross-sectional study was conducted at National Institute of Cardiovascular Disease (NICVD) Karachi, Pakistan after approval of ethical review committee of the Institute from 1st May to 30th September 2017. Patients above 20 years of age, admitted to adult cardiology department with ECG evidence of paroxysmal, persistent or permanent Atrial fibrillation(AF) with no structural heart defect like valvular or congenital, hypertrophic and restrictive cardiomyopathy or constrictive pericarditis, without any thyroid dysfunction or active malignancy and having no indications of anticoagulation other than AF were selected. Informed consent was taken explaining purpose, procedure, risks and benefits of the study. Demographic profile and clinical history was obtained for all the patients. The thromboembolic risk of individual patients was stratified according to the CHA₂DS₂-VASc score. The CHA₂DS₂-VASc score was calculated by assigning 1 point each for congestive heart failure/left ventricular systolic dysfunction (left ventricular ejection fraction [LVEF] ≤40%), hypertension, diabetes, vascular disease (including prior myocardial infarction [MI] or definitive evidence of peripheral

vascular disease), age 65 years, and female gender, and 2 points for prior thromboembolism/Transient Ischemic Attack/stroke and for age ≥75 years. Information about different types of therapies or medication like warfarin, Novel oral anticoagulants(NOACs), etc. was obtained from all the patient with level of international normalization ratio(INR) for those on Warfarin to assess their adequacy of anticoagulation.

Non valvular AF patients with CHA₂DS₂-VASc score more than or equal to 2 were considered high risk and patients on Warfarin with their last INR between 2 to 3 were labeled adequately anticoagulated.

Statistical package for social sciences (SPSS 21) was used to analyze the data. Mean ± SD was calculated for quantitative variables and frequency and percentages for categorical variables. Chi-square test or t-test was applied for the assessment and comparison of categorical or continuous variables respectively. Two-sided p-value of ≤0.05 was taken as criteria for statistical significance.

RESULTS

Out of 160 total patients majority were males (52.5%) and up to 65 years of age (52.5%). Hypertension followed by history of congestive heart failure were the most common clinical conditions. Mean ± standard deviation of the CHA₂DS₂-VASc score was 3.14 ± 1.56. The baseline characteristics and factors constituting CHA₂DS₂-VASc score (Table 1).

Out of 160 patients, 137 found to be at high risk, 86 of them were taking warfarin while 18 were on NOACs, and those on warfarin only 18 patients were adequately anticoagulated that is having INR of 2-3. Percentage of them in total patients and different gender is shown in figure 1.

The details of different antithrombotic treatment prescribed to high and low risk patients and their level of INR if taking warfarin as shown in table 2. One important finding in this table was that even 17 (73.9%) out of 23 low risk patients were also prescribed Warfarin relative percentage of which is more than 86(62.8%) out of 137 high risk patients who were on warfarin.

Table 1 : Baseline Characteristics of Patients Presented with Atrial Fibrillation (n = 160)

Variables	n [%]
Gender	
Male	84 [52.5%]
Female	76 [47.5%]
Age (years)	
Mean ± SD	60.34 ± 11.91
Less than 65 years	84 [52.5%]
65 to 74 years	63 [39.4%]
≥ 75 years	13 [8.1%]
Married	155 [96.9%]
Clinical History	
Congestive Heart Failure(CHF)	89 [55.6%]
Hypertension	97 [60.6%]
Diabetes	30 [18.8%]
Stroke / TIA /TE	27 [16.9%]
Vascular Disease	67 [41.9%]
Thromboembolic Risk	
Low Risk (CHA ₂ DS ₂ VASc score < 2)	23 [14.4%]
High Risk (CHA ₂ DS ₂ VASc score > 2)	137 [85.6%]

SD = Standard Deviation, TIA = Transient Ischemic Attack, TE = Thromboembolism

Figure 1: Risk of Thromboembolism & Adequacy of Anticoagulation (n=160)

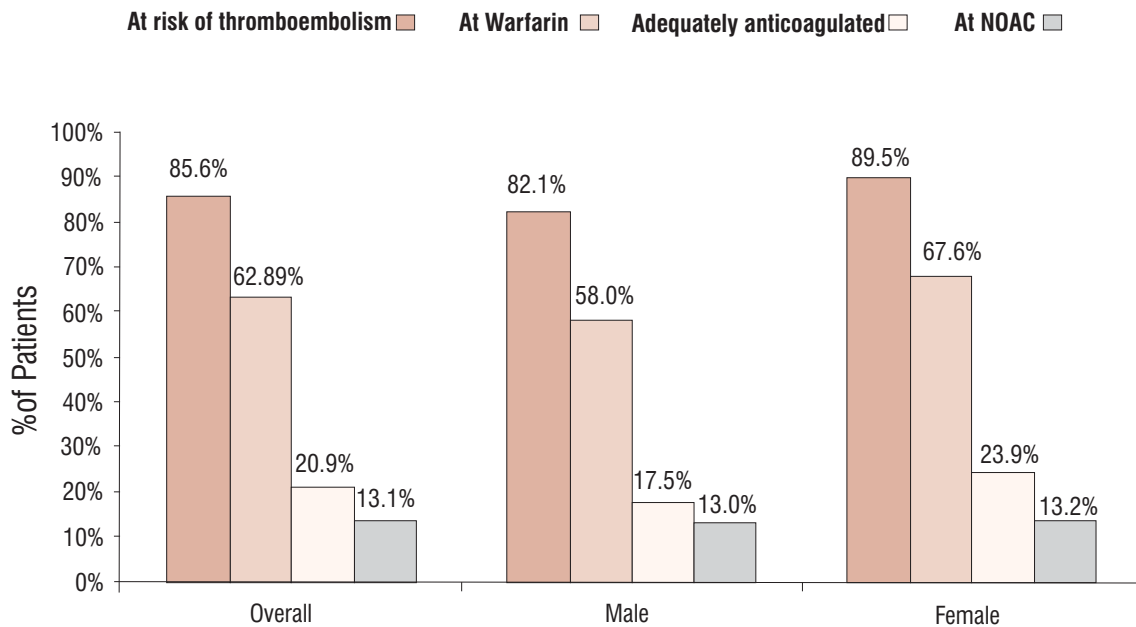


Table 2 : Antithrombotic Treatment by Risk of Atrial Fibrillation (n=160)

Variable	n (%)	Thromboembolic Risk		P-value
		Low Risk (n = 23)	High Risk (n = 137)	
Present Antithrombotic Treatment				
Aspirin	120 [75.0%]	17 [73.9%]	103 [75.2%]	0.896
Clopidogrel	28 [17.5%]	3 [13.0%]	25 [18.2%]	0.543
Warfarin	103 [64.4%]	17 [73.9%]	86 [62.8%]	0.301
NOAC	18 [11.3%]	0 [0%]	18 [13.1%]	0.065
**INR Value				
Less than 2	53 [51.5%]	7 [41.2%]	46 [53.5%]	0.428
2 to 3	24 [23.3%]	6 [35.3%]	18 [20.9%]	
More than 3	26 [25.2%]	4 [23.5%]	22 [25.6%]	
**Dosage / Week				
< 20mg	17 [16.5%]	3 [17.6%]	14 [16.3%]	0.954
20-35mg	58 [56.3%]	9 [52.9%]	49 [57.0%]	
> 35mg	28 [27.2%]	5 [29.4%]	23 [26.7%]	

*Statistically significant at 5% level of significance

** INR and Dosage breakup is based on 103 patients on Warfarin (17 low risk and 86 high risk)

DISCUSSION

Risk of thromboembolism is significantly higher among the patients with Atrial Fibrillation (AF). Over the years a number of risk stratification modalities and scoring schemas have been developed in order to identify and stratify the patients at higher risk for the customized management accordingly. CHADS2 scoring system is one such widely used and accepted risk stratification modality, which was initially computed considering known risk factors such as diabetes mellitus (DM), hypertension (HTN), advanced age (more than 75 years), congestive heart failure (CHF), or past history of stroke/transient ischemic attack (TIA). ACC/AHA guidelines 2014 recommended the updated CHA₂DS₂VASc score. The updated CHA₂DS₂VASc score, along with known risk factors, also consider female gender and vascular disease for the calculation of risk score.⁷

In our part of the world, candidate patients for anticoagulation are improperly or inadequately treated with anticoagulation. These patients were either given antiplatelet medication rather than anticoagulation or not put on any medication therapy. There are number of reasons reported in literature for this noncompliance of anticoagulation. Most of those reasons include lack of awareness of disease, low literacy rate, low awareness regarding importance of anticoagulation, lack of access to the health care professionals and facilities, poverty and financial constraints, and unable to maintain the effective therapeutic range (INR) as a result of multiple factors.¹⁷⁻¹⁹

Our study showed majority of patients about 85.6% (137) with non valvular AF were found to be at high risk of thromboembolism. Warfarin was prescribed in 64.4% (103) patients and 13.1% (18) of high risk patients were taking Rivaroxiban as well. Another local study conducted by Ikramullah et al. on similar patients group found to have 27%

of patients on anticoagulation and a French study conducted by Tavassoli N et al. on older patients with atrial fibrillation with two or more risk factors for stroke, found 50% patients on warfarin therapy.^{20,21} One more similar study conducted by Tanislav C et al. found that only 45% patients with AF with high risk of stroke were receiving anticoagulation therapies.²² Our percentage of patients was better in terms of receiving Anticoagulants probably because of a good number of them were recruited from dedicated INR clinic.

One more finding which is a bit alarming as well is out of those high risk patients on warfarin only 18 (20.9%) found to have adequate anticoagulation, which is clearly raise red flags about oral anticoagulant therapy specially warfarin that, in spite of being prescribed to a good percentage only a few were able to achieve desirable goal. We saw some trends of prescribing NOACs (Rivaroxiban) in our study as well, which may be a good alternative to the problem we are facing with Warfarin in achieving adequate anticoagulation. Our study sample was small and was done at tertiary care center so cannot portray a true picture of what's happening in the community.

CONCLUSION

Our study showed that a majority of patients with non-valvular AF are at higher risk of thromboembolism with inadequate anticoagulation. It is of profound importance to assess the risk of thromboembolism in every patient with non-valvular AF and achieving adequate anticoagulation should be the goal apart from prescribing anticoagulants to reduce stroke risk. NOACs can be a good alternative in this regard.

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