

Anticoagulation use and predictors of stroke, bleeding and mortality in multi-ethnic Asian patients with atrial fibrillation: A single centre experience

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ABSTRACT

Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia in Singapore. We describe a cohort of multi-ethnic Asian patients with AF, with the aim to evaluate anticoagulation use and to identify factors predictive of stroke, bleeding and all-cause mortality.

Materials and Methods: This was a single centre, retrospective cohort study. All patients with an admission diagnosis of AF between 1 January 2000 and 31 December 2010 were identified. Of these patients, those who had follow-up data up to 31 December 2012 were included in the study.

Results: There were 1095 eligible patients. The mean age was 67±14 years, mean CHADS2 score was 2±1 and mean HAS-BLED score 2±1. Of the 1095 patients, 657 (62.0%) had a CHADS2 score ≥ 2 but only 215 (32.7%) were eventually prescribed warfarin. Patients not on warfarin were older ($p<0.0001$) and were more likely females ($p<0.0001$). Among patients not on warfarin, 52% had HAS-BLED score ≤3. Multivariate analysis revealed that warfarin use and high HAS-BLED score were associated with increased bleeding risk. Age, Indian ethnicity and CHADS2 score were predictive of ischemic stroke. All-cause mortality was significantly related to age, presence of heart failure and HAS-BLED score.

Conclusions: Anticoagulation management of AF patients remains inadequate. Objective assessment of bleeding risks should be performed before withholding anticoagulation.

KEY WORDS:

Atrial fibrillation; Stroke; Anticoagulation

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia in Singapore with a reported estimated prevalence of 1.5% in adults based on electrocardiography documentation.¹ As the population ages, the prevalence of AF is expected to increase. AF is associated with up to five times increased risk of stroke which tends to be more severe when compared to stroke from other causes.^{2,3} The CHADS2 and more recently, the CHADS-Vasc scores, can be used to stratify stroke risk and need for anticoagulation in AF

patients.⁴ The HAS-BLED score is useful to objectively evaluate bleeding risk prior to initiation of anticoagulation.^{4,5}

Anticoagulation therapy remains the cornerstone for stroke prevention in AF patients. However, it is withheld in many patients due to bleeding concerns. We describe the baseline clinical characteristics of a cohort of multi-ethnic Asian patients with AF, with the aim to identify factors predictive of stroke, bleeding and all-cause mortality. We also evaluated anticoagulation use in this patient cohort.

MATERIALS AND METHODS

This was a single centre, retrospective cohort study. All patients who were admitted to our tertiary hospital with an admission diagnosis of AF between 1 January 2000 and 31 December 2010 were identified. These included patients hospitalized under Cardiology and non-Cardiology departments. Of these patients, those who had follow-up data up to 31 December 2012 were enrolled in the study.

Patient demographics and clinical data were obtained through a review of their medical case records. The incidences of ischemic stroke, major bleeding and all-cause mortality were recorded. Ischemic stroke was defined as a focal neurological deficit lasting 24 hours or more and proven on brain imaging. As per the International Society on Thrombosis and Haemostasis (ISTH) criteria, major bleeding was defined as a reduction in hemoglobin level of at least 2g per deciliter or transfusion of at least two units of packed red cells or clinically apparent bleeding at a critical site or resulting in death.⁶ CHADS2 and HAS-BLED scores were calculated for each patient. The CHADS-Vasc score was not computed as it was not routinely used in our institution for stroke risk stratification between 2000 and 2012.

The chi-square test was used to compare categorical variables and the unpaired t test used for comparison of continuous variables. We used the logistic regression model to identify variables that were significantly and independently associated with ischemic stroke, major bleeding and all-cause mortality. The backward likelihood test with probability of removal set at 5% was used for the multivariate model. Data analysis was performed in Stata V11 (Stata Corp, College Station, Tx, USA) and level of significance set at 5%.

This article was accepted: 11 August 2016

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Table I: Baseline clinical characteristics of patients

	n=1095
Clinical characteristics	
Age (years)	67±14
Male	480 (43.8%)
Chinese	873 (79.7%)
Malay	187 (11.1%)
Indian	74 (4.4%)
Diabetes mellitus	314 (28.7%)
Hypertension	746 (68.1%)
History of stroke	179 (16.4%)
History of heart failure	350 (31.9%)
Coronary artery disease	389 (35.5%)
Thyrotoxicosis	50 (4.6%)
Newly diagnosed atrial fibrillation	648 (59.2%)
Classification of atrial fibrillation	
- Paroxysmal	743 (67.9%)
- Persistent	82 (7.5%)
- Permanent	269 (24.6%)
Main presenting symptoms	
- Palpitations	419 (38.3%)
- Dyspnoea	214 (19.6%)
- Chest pain	179 (16.4%)
- Dizziness	108 (9.9%)
- Asymptomatic	61 (5.6%)
- Syncope	29 (2.65%)
Mean CHADS2 score	2±1
Mean HASBLED score	2±1
CHADS2 score ≥ 2	657 (62.0%)
On warfarin therapy	353 (32.2%)
On antiplatelet therapy	684 (62.5%)

RESULTS

There were 1095 eligible patients and 480 (43.8%) were male. Table 1 summarizes the baseline clinical characteristics of these patients. There were 873 (79.7%) Chinese, 187 (11.1%) Malays and 74 (4.4%) Indians. The mean age was 67±14 years, mean CHADS2 score was 2±1 and mean HAS-BLED score 2±1. Diabetes mellitus was present in 314 (28.7%) patients, 746 (68.1%) had hypertension, 179 (16.4%) previous stroke, 350 (31.9%) had a history of congestive cardiac failure, 50 (4.6%) had thyrotoxicosis. The commonest 3 presenting symptoms were palpitations (38.3%), dyspnoea (19.6%) and chest pain (16.4%).

Newly diagnosed AF cases numbered 648 (59.2%), 743 (67.9%) were labelled as paroxysmal AF, 269 (24.6%) as permanent AF. Warfarin was prescribed in 353 (32.2%) patients and 684 (62.5%) received anti-platelet therapy. Over a mean follow-up period of 7.5 ± 5.5 years, 126 (11.5%) patients developed ischemic stroke, 91 (8.3%) had major bleeding complications and 127 (11.6%) died.

Of the 1095 patients, 657 (62.0%) had a CHADS2 score ≥ 2 and were eligible for warfarin therapy. Of these 657 patients, 215 (32.7%) were prescribed warfarin and 442 (67.3%) were not. Comparing the 2 groups, patients not on warfarin were older (mean age 75±12 years vs 68±10 years; $p<0.0001$) and were more likely females (63% vs 56%; $p<0.0001$). There was no significant difference in the HAS-BLED scores between the 2 groups (2.5±1 vs 2.4±1; $p=1$). Among patients not on warfarin, 52% had HAS-BLED score ≤3.

Multivariate analysis revealed that warfarin use (OR=2.58; 95% CI: 1.62-4.12) and high HAS-BLED score (OR=1.44; 95% CI: 1.21-1.71) were associated with increased bleeding risk. Age (OR=1.02; 95% CI: 1.0-1.04), Indian ethnicity (OR=2.16; 95% CI: 1.03-4.54) and CHADS2 score (OR=1.18; 95% CI: 1.02-1.37) were predictive of ischemic stroke. All-cause mortality was significantly related to age (OR=1.05; 95% CI: 1.03-1.07), presence of heart failure (OR=2.01; 95% CI: 1.35-2.99) and HAS-BLED score (OR=1.24; 95% CI: 1.06-1.46).

DISCUSSION

Interestingly, we found that Indian AF patients were significantly more likely to develop ischemic stroke. This finding is hypothesis-generating in that with the same CHADS2 score, the risk of ischemic stroke in AF may be variable across ethnic groups in Singapore. It has been reported that Indians have a higher prevalence of stroke risk factors such as cigarette smoking, hypertension and hypercholesterolemia.⁷ However, it is not known whether these risk factors alone can account for the higher ischemic stroke risk or if genetic factors play any role.

In AF patients from 44 countries across Europe, Americas and Asia, the rate of warfarin use has been shown to be 53%, with the rate in Southeast Asia ranging from 25.5% to 52.9%. Singapore was reported to have a rate of 35.8%.^{8,9} Our finding of warfarin underuse in our patient cohort (32.2%) was not unexpected and appeared to be consistent with published data.

Based on CHADS2 score, 62% of our patients required warfarin therapy for stroke prevention but only 32.7% of these patients were prescribed warfarin. Elderly women were less likely to be given warfarin, presumably because of perceived high bleeding risks. However, using the HAS-BLED score to objectively evaluate bleeding risks in these patients, at least half of these patients had low bleeding risk with a score of ≤ 3 . Instead of making clinical decisions based on preconceived notions, this finding underscored the importance of proper objective evaluation of bleeding risks in each individual before deciding against anticoagulation.

The underuse of anticoagulation in AF patients has been a long-standing conundrum, involving an inter-play of physician and patient factors. The introduction of novel anticoagulants, with the convenience of administration and lower rates of intracranial hemorrhage, may help ameliorate the problem. The availability of patient self-testing kits for International Normalized Ratio is another step in the right direction. Most importantly, physicians and patients alike should be provided with all the necessary education and tools to help them make the best informed decision on anticoagulation for stroke prevention.

Our study had a number of limitations. Due to the retrospective cohort study design, our findings were at most hypothesis-generating. We were not able to determine the actual reasons for anticoagulation underuse as the reasons for withholding warfarin were frequently not clearly documented in many patients' case records.

CONCLUSION

Inadequate use of anticoagulation among AF patients remains a major issue for stroke prevention. Objective assessment of bleeding risks should be performed before making a clinical decision to withhold anticoagulation. Stroke risk may be different across various ethnic groups with similar CHADS2 scores and more research would be necessary in this area.

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