

Underutilisation of Guideline-based Therapy Primary Prevention among Patients Presenting with AF-related Ischaemic Stroke

Dear Editor,

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia with a prevalence of 1.5% in Singapore and 0.4% to 1% in the general population.¹ The risk of ischaemic stroke in patients with AF is increased by fivefold² and is stratified using CHA₂DS₂-VASc score.³ AF-related strokes are associated with greater disability and mortality.^{4,5}

Anticoagulation with warfarin and novel oral anticoagulation (NOAC) drugs significantly decreases the risk of stroke and is recommended for most patients with AF. Antiplatelet therapy also decreases stroke risk for low-risk patients but is less effective than anticoagulation.⁶

In published literature, utilisation of anticoagulation for primary stroke prevention is limited because of over-concern for bleeding risks,⁷ however, there are no data on the local situation in Singapore. We aimed to study patients admitted with AF-related stroke in a tertiary hospital in Singapore to describe 1) the frequency of previously known and newly diagnosed AF; 2) distribution of CHA₂DS₂-VASc score prestroke and postindex-stroke and its association with total anterior circulation infarction (TACI) by Oxfordshire Community Stroke Project (OCSP) classification as a marker of severe and large stroke; and 3) utilisation of appropriate primary stroke prevention in patients with previously known AF and secondary stroke prevention strategies on discharge.

Materials and Methods

This is an observational prospective study of consecutive AF-associated ischaemic stroke patients admitted to Singapore General Hospital from January 2012 to November 2012. The inclusion criteria were acute ischaemic stroke with previously known or newly diagnosed AF as the cardioembolic source.

Data was obtained from medical records during the acute stroke hospitalisation. Neurological severity was assessed by ward nurses who were certified for the National Institutes of Health Stroke Scale (NIHSS).⁸ The CHA₂DS₂-VASc score was calculated for 2 time points: prestroke based on data at admission and postindex-stroke based on data at discharge. We defined a high stroke risk as CHA₂DS₂-VASc score >5 which carries an annual risk of 9.8% to 15.2% compared to 1.4% to 6.7% for a score of ≤5.⁹ Stroke subtype was

classified using OCSP with TACI as surrogate for severe and large stroke.⁵

For evaluation of antithrombotic use, warfarin and the NOACs dabigatran, rivaroxaban and apixaban were considered oral anticoagulants while aspirin, dipyridamole, ticlopidine and clopidogrel were antiplatelet drugs. Double-antiplatelet therapy was defined as concomitant use of aspirin + clopidogrel or aspirin + dipyridamole. If patients were on warfarin prestroke, the international normalised ratio (INR) was noted and a range of 2 to 3 being therapeutically optimal.⁹

Statistical analyses were performed with SPSS software version 17.0. Descriptive data were presented as frequencies. Chi-square test was employed to determine the relationship between dichotomous variables. This study was approved by the institutional review board and waiver of consent was obtained.

Results

Among the 60 patients with AF-related ischaemic stroke, mean age was 74.2 ± 9.4 years and median NIHSS score was 4 (interquartile range (IQR) = 11). Nine (15%) had TACI, 21 (35%) had partial anterior circulation infarction (PACI), 7 (12%) had posterior circulation infarction (POCI), 22 (37%) had lacunar infarction (LACI) and 1 had no OCSP data. Forty-seven (78%) had previously known AF prestroke and 13 (22%) had AF diagnosed during admission. All patients with previously known AF had a pre-admission CHA₂DS₂-VASc score of >1 with a median of 4 (IQR = 2). On discharge the median score was 6 (IQR = 2). Among 13 patients with newly diagnosed AF, the median pre-admission CHA₂DS₂-VASc was 4 (IQR = 2) and 6 (IQR = 2.5) on discharge. Prior to admission, 11 (18%) had CHA₂DS₂-VASc score of >5, while 49 (82%) had a score of ≤5. The proportion of patients with TACI was higher among those with CHA₂DS₂-VASc score of >5 (5 out of 11; 46%) versus those with a score of ≤5 (4 out of 49; 8.3%, *P* = 0.008). Upon recalculation of the CHA₂DS₂-VASc score on discharge, 32 (53%) scored >5, while 28 (47%) scored ≤5.

Prestroke and poststroke antithrombotic use per CHA₂DS₂-VASc score among patients with previously known AF is

shown in Figure 1. Only 10 (21%) out of 47 previously known AF patients were on anticoagulation on admission, with only 3 (30%) of these 10 having a therapeutic INR. Twenty-nine (62%) of them were on antiplatelet, 2 (4%) were on double-antiplatelet while 6 (13%) were not on any antithrombotic medication. Overall, on discharge, 30 (50%) of the 60 patients were on oral anticoagulants [24 (40%) on warfarin, 6 (10%) on NOACs], 18 (30%) were on antiplatelet agents, 5 (8%) were on double-antiplatelet, 1 (2%) was on concomitant use of warfarin + clopidogrel and 6 (10%) were not on any antithrombotic medication. Of the 37 patients with previously known AF and not on anticoagulation pre-admission, 16 (43%) were prescribed anticoagulation on discharge [12 (75%) with warfarin and 4 (25%) with NOACs], 12 (32%) were on antiplatelet, 5 (14%) were on double-antiplatelet and 4 (11%) were not on any antithrombotic medication.

Discussion

This study found that most (79%) of the patients with known AF presenting with ischaemic stroke were not on appropriate anticoagulation, similar to many studies in developing countries such as Malaysia (16%) and China (2.7% to 50%).² Utilisation of anticoagulation for primary stroke prevention can be optimised as evidenced by a much higher rate of 85% in Europe.¹⁰ Our data suggest that locally there is much room for improvement in primary stroke prevention in patients with AF. There is a known interplay between the risks and benefits of anticoagulants.⁷ This study's finding that nearly half of known AF patients

not on anticoagulation pre-admission were discharged with anticoagulants illustrates that they had no absolute contraindication and confirms missed opportunities for primary stroke prevention.

Potential strategies to improve utilisation of anticoagulation for primary stroke prevention in AF include employing risk stratification tools.^{3,11} The CHA₂DS₂-VASc score, a predictor of stroke risk in AF,³ is also associated with stroke severity as confirmed by our finding that more patients with a score of >5 had TACI which is known to have a very poor prognosis.⁴ The HAS-BLED score predicts risk of haemorrhage with anticoagulation¹¹ and is high in individuals with high CHA₂DS₂-VASc score due to common factors. However, it should be noted that the risk reduction with anticoagulation is higher in those with higher CHA₂DS₂-VASc and HAS-BLED scores^{9,12} and HAS-BLED is proposed to recognise, address and manage factors of haemorrhagic risk rather than to restrict the use of anticoagulation.⁹

Only a small proportion of our stroke patients with known AF on warfarin had therapeutic INR (30%) which is similar to that in developing countries (30% to 50%).² Possible reasons for this include increased stroke risk with subtherapeutic INR⁹ and low time in therapeutic range (TTR).¹³ Of note, none of the patients with previously known AF who were on anticoagulation were on NOACs. This offers a potential opportunity other than warfarin especially where bleeding complications, compliance and reluctance of blood monitoring are issues. Although concern has been expressed about patient adherence, lack of specific antidotes, increased cost and not being widely

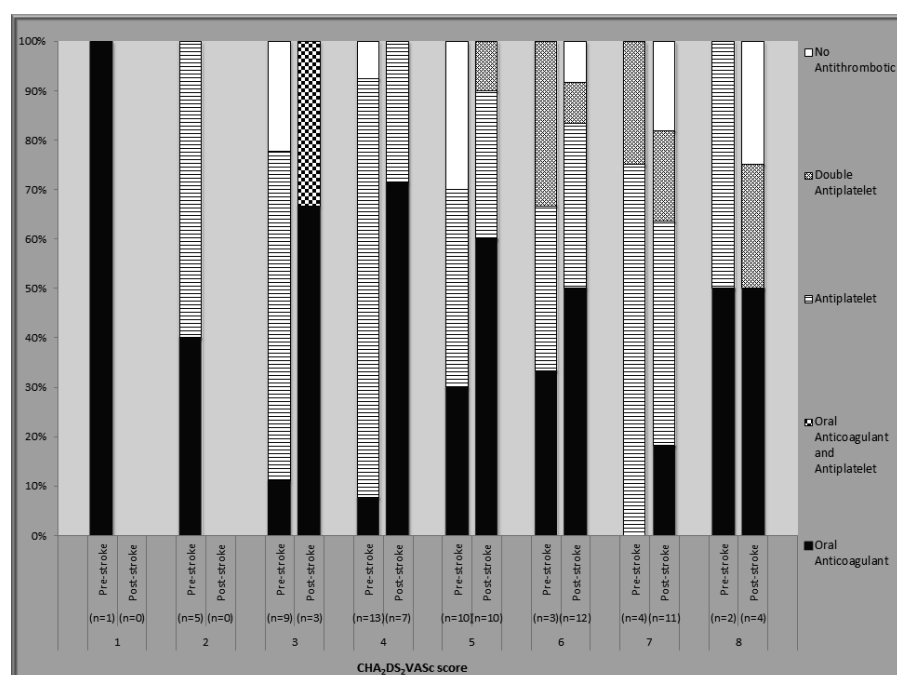


Fig. 1. Prestroke and poststroke antithrombotic use per CHA₂DS₂-VASc score among patients with previously known AF.

available, NOACs are as effective as warfarin for stroke prevention in non-valvular AF, with better haemorrhagic safety profiles and convenience of use.¹⁴

Strengths of this study include assessment of CHA₂DS₂-VASc score in both pre and post-stroke settings to assess optimal treatment as well as collation of anticoagulation use on discharge as a surrogate for the lack of absolute contraindications. The main limitation of this study is that being a chart review, the reasons for non-utilisation of anticoagulation were not readily enumerated, thus the absolute and relative contraindications were not assessed. NICE consensus recommends that local arrangements for use of antithrombotic therapies in AF should be reviewed and policies developed for integration of NOACs into the care pathway.¹⁴ We did not collate data on whether the AF was paroxysmal or permanent, or the mode of detection of AF. In addition, being a single centre study may lend bias. However, as Singapore's population is homogeneously distributed, these data are likely generalisable.

Conclusion

There was very limited use as well as clearly missed opportunities for appropriate optimal anticoagulation in known AF patients presenting with ischaemic stroke in this study, advocating the need for improvement of primary stroke prevention in AF in Singapore.

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