

# Stroke prevention in atrial fibrillation: the Singapore story

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**A**trial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. In 2008, Yap et al estimated that the overall AF prevalence in Singapore was 1.5%, and this would have increased over the years with our ageing population.<sup>(1)</sup> AF results in a twofold rise in mortality and a fivefold increase in the risk of stroke. The overall annual incidence of AF-associated ischaemic stroke in Asia ranged from 1.3% in Japan to 15.4% in the Far East and Southeast Asia.<sup>(2,3)</sup> Ischaemic stroke in AF patients typically causes a greater degree of disability and higher mortality. Consequently, AF is increasingly recognised as a significant public health concern, given its negative impact on morbidity and mortality.

The cornerstone of stroke prevention in AF is anticoagulation. The Asia Pacific Heart Rhythm Society (APHRS) consensus guideline recommends the CHA<sub>2</sub>DS<sub>2</sub>-VASc score for the prediction of stroke risk in Asians with non-valvular AF.<sup>(4)</sup> Oral anticoagulation is recommended for males with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 1$  and females with a score  $\geq 2$ , with non-vitamin K antagonist oral anticoagulants (NOACs) being preferred over warfarin.

In this issue of the *Singapore Medical Journal*, Krittayaphong et al highlighted the problem of suboptimal anticoagulation therapy with warfarin for stroke prevention in AF patients in Thailand.<sup>(5)</sup> Due to the higher costs of NOACs, warfarin remains a widely prescribed oral anticoagulant in Asia, including Singapore. The efficacy and safety of warfarin is dependent on the quality of international normalised ratio (INR) control, as measured by the time in therapeutic range (TTR). A TTR  $< 60\%$  reflects poor quality of warfarin treatment and is linked to increased patient mortality and adverse outcomes. Bernaitis et al reported an overall mean TTR of 58% in AF patients receiving warfarin in a tertiary cardiac centre in Singapore, with a TTR in Chinese, Malays and Indians of 58.7%, 55.2% and 49.7%, respectively.<sup>(6)</sup> Kew et al showed that up to 61.3% of AF patients at high risk of cardioembolic stroke were not prescribed warfarin upon discharge from a tertiary cardiology unit in Singapore.<sup>(7)</sup> The most common reasons for withholding anticoagulation were physicians' decisions, patients' turning it down and history of bleeding. Aribou et al debunked some fears that physicians in Singapore faced during anticoagulation prescribing, such as advanced age, fall and bleeding risks, providing evidence that these concerns were largely unfounded.<sup>(8)</sup>

The issue of having poor-quality anticoagulation with warfarin is not unique to Singapore and Thailand. The Global Anticoagulant Registry in the Field-Atrial Fibrillation revealed that patients from Eastern and Southeastern Asian countries recorded significantly lower TTR (31.1% vs. 54.1%) compared to the rest of

the world.<sup>(9)</sup> To help identify Asian patients who are likely to have suboptimal TTR, the APHRS consensus guideline recommends the use of the SAME-TT<sub>2</sub>R<sub>2</sub> score (i.e. sex, age, medical history, treatment, tobacco use, race).<sup>(4)</sup> In Singapore, Bernaitis et al validated the SAME-TT<sub>2</sub>R<sub>2</sub> score in a retrospective study, reporting that a score  $\geq 3$  predicted a TTR  $< 60\%$ .<sup>(6)</sup> Such patients were less likely to achieve good quality anticoagulation with warfarin, and alternative anticoagulants such as NOACs should be considered.

The use of NOACs in Singapore has increased steadily since their introduction in 2011. Compared to warfarin, the main advantages of NOACs are fewer interactions with other drugs and foods, reduced risk of intracranial bleeding, quick onset and offset of action that obviates the need for bridging therapy during anticoagulation interruption, and no requirement for regular INR monitoring. Reversal agents have also become available: andexanet alfa for Factor Xa inhibitors (rivaroxaban, apixaban and edoxaban) and idarucizumab for the direct thrombin inhibitor dabigatran. In a meta-analysis comparing Asians and non-Asians, Wang et al reported that standard-dose NOACs were more effective in reducing stroke or systemic embolism and resulted in significantly less major bleeding in Asians.<sup>(10)</sup> The efficacy and safety of NOACs in AF patients in Singapore have been described in two local studies.<sup>(11,12)</sup>

In line with international guidelines, NOACs should therefore be the anticoagulant of choice in Singapore for stroke prevention in patients with non-valvular AF.<sup>(4,13,14)</sup> The main impediment to NOAC use is higher prices when compared with warfarin. However, the introduction of government subsidies has helped to offset the drug costs, which may decrease with the possible introduction of generic versions in 4–5 years. Warfarin still has a role in special AF patient populations, namely those with Stage 4 and 5 chronic kidney disease, moderate to severe mitral stenosis and patients with mechanical heart valves.<sup>(4,13,14)</sup> A SAME-TT<sub>2</sub>R<sub>2</sub> score  $\geq 3$  can help to identify patients who will require more frequent clinic reviews, INR monitoring, education and counselling to ensure optimal TTR.

## REFERENCES

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