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**EDITORIAL**

# Simple decision-making between a vitamin K antagonist and a non-vitamin K antagonist oral anticoagulant: using the SAMe-$TT_2R_2$ score

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Stroke prevention with oral anticoagulation (OAC) is central to the modern management of atrial fibrillation (AF) patients.[1] For many years, vitamin K antagonists (VKAs, e.g. warfarin) have been the default class of OAC, but we now recognize that it is not simply prescribing VKA but very close attention to quality of anticoagulation control is necessary, as reflected by the individual time in therapeutic range (TTR).[2] An average individual TTR of >70% is recommended to maximize efficacy and safety of the VKAs.[2,3]

Nonetheless, the VKAs have significant inter- and intra-patient variability, partly from diet and drug interactions, thus necessitating regular international normalised ratio (INR) monitoring.[2] More recently, we have had the non-VKA oral anticoagulants (NOACs, previously referred to as new or novel OACs[4]) available, which offer efficacy, safety, and relative convenience compared with the VKAs, for stroke prevention in AF.

Due to cost considerations, some healthcare systems mandate a 'trial of warfarin' (sometimes called a 'warfarin stress test') for the initial 6 months, to determine whether a patient can do well on a VKA—and only if the TTR is suboptimal (e.g. <60%) is an NOAC then 'authorized' to be prescribed. When a patient is first started on a VKA, the inception period is often associated with a poor TTR, and an excess of thromboembolism has been noted in various studies.[5,6]

A major challenge therefore is to easily identify those AF patients who are less likely to do well on a VKA (with a poor TTR) who may be best switched to an NOAC, rather than being exposed to suboptimal TTRs and inadequate thromboprophylaxis, exposing the patient to fatal and disabling strokes. Also, some healthcare settings have a good track record of managing VKA very well, achieving (very) high TTRs. Thus, rather than using guesswork (or budget considerations) to decide between a VKA and an NOAC in a newly diagnosed anticoagulation-naive patient, the SAMe-$TT_2R_2$ score was proposed to aid such decision-making (Table 1).[7]

The SAMe-$TT_2R_2$ score is a relatively simple clinical risk score to help decision-making in our everyday practice, whereby those patients with a SAMe-$TT_2R_2$ score of 0–2 are *on probability* likely to achieve a high TTR and thus, a VKA can be prescribed upfront.[7] In contrast, a SAMe-$TT_2R_2$ score of >2 is associated with a poor TTR, and as patients are less likely to do well on a VKA (thus, exposing them to more thromboembolism and bleeding), and intense efforts to improve TTR by education[8] or choosing an NOAC would be better initial options.

In various independent cohorts, the SAMe-$TT_2R_2$ score has shown a good capacity to discriminate patients with a good TTR (e.g. >65–70%; Table 2).[9–11] Moreover, the SAMe-$TT_2R_2$ score has proved to be valuable in predicting labile INRs, leading to both adverse bleeding and thromboembolic events.[10–12] Thus, robust evidence is accumulating from large cohort studies of the value and clinical application of using this simple score. Smaller, underpowered cohorts with only a narrow range of INRs in the cohort studied have shown less impressive results.[13]

The most recent validation study was published by Abumuaileq *et al.*[11] and demonstrated the ability of SAMe-$TT_2R_2$ score to identify patients even with a high TTR cut-off point (≥70%), and since poor TTR is related to more adverse effects, the score was also predictive of all-cause mortality and the composite endpoint of major bleeding, thromboembolic complications, and mortality.[11] Indeed, their data are consistent with other prior studies from Italy,[9] Spain,[10] and France.[12] Thus, there is increasing evidence for the utility of the SAMe-$TT_2R_2$ score, in helping the patient management pathway.

Of note, the SAMe-$TT_2R_2$ score is recommended in the UK National Institute for Health and Care Excellence (NICE) NOAC Implementation Collaborative consensus document (http://www.nice.org.uk/guidance/cg180/resources) and also has been proposed in the PRIMIS' development of the Warfarin Patient Safety audit tool (http://www.nottingham.ac.uk/primis/tools/audits/warfarin-patient-safety.aspx). The ESC Working Group on Thrombosis Anticoagulation Task Force also recommends the use of SAMe-$TT_2R_2$ score to aid decision-making between a VKA and an NOAC, in a newly diagnosed anticoagulation-naive patient with AF. A suggested patient pathway for using the score in a newly diagnosed, non-anticoagulated AF patient is shown in *Figure 1*.

With the NOACs, we cannot check INRs or the equivalent of a parameter such as the TTR,[14,15] and thus, we perhaps lose one

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**Table 1** SAMe-$TT_2R_2$ score

| | Definitions | Points |
|---|---|---|
| S | Sex (female) | 1 |
| A | Age (<60 years) | 1 |
| Me | Medical history[a] | 1 |
| T | Treatment (interacting drugs, e.g. amiodarone for rhythm control) | 1 |
| T | Tobacco use (within 2 years) | 2 |
| R | Race (non-Caucasian) | 2 |
| Maximum points | | 8 |

[a]More than two of the following: hypertension, diabetes, coronary artery disease/myocardial infarction, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, and hepatic or renal disease.

powerful tool to predict anticoagulation quality in AF patients. Could the SAMe-$TT_2R_2$ score achieve more beyond the prediction of TTR cut-off points, perhaps by being a 'TTR surrogate' that informs the clinical likelihood of achieving good quality anticoagulation control, in a patient started on an NOAC? Further studies are needed to test this hypothesis.

We can certainly encourage further observational studies planned to evaluate the predictive power of SAMe-$TT_2R_2$ score, both in its original and revised form, in predicting major bleeding and thromboembolic complications, even beyond TTR assessment. A prospective randomized trial, evaluating the impact of SAMe-$TT_2R_2$ score-guided therapy with VKA or NOAC, would also allow us to formalize its clinical utility, and is stated as a research recommendation in the 2014 NICE guidelines for AF.[16] Ultimately, clinicians need simple clinical tools to aid decision-making in everyday clinical practice, and not rely on complex formulae based on multivariate models that were derived from a specific selected population or a trial cohort. The

**Table 2** SAMe-$TT_2R_2$ validation studies

| | Study design | Patients | Follow-up time | SAMe-$TT_2R_2$ distribution |
|---|---|---|---|---|
| Apostolakis *et al.*[7] | Retrospective | 1305 AF | NA | Score 0–1: 655 pts<br>Score 2: 303 pts<br>Score >2: 347 pts |
| Skov *et al.*[13] | Prospective | 182 | 1 year | Score 0–1: 105<br>Score ≥2: 77 |
| Poli *et al.*[9] | Prospective | 1089 AF | 4.6 years (mean) | Score 0–1: 624 pts<br>Score 2: 288 pts<br>Score >2: 177 pts |
| Gallego *et al.*[10] | Prospective | 972 NVAF | 952 days (median) | Score 0–1: 431 pts<br>Score 2: 332 pts<br>Score >2: 208 pts |
| Lip *et al.*[12] | Prospective | 8120 AF | 1016 days (mean) | Score 0–1: 4504 pts<br>Score 2: 2252 pts<br>Score >2: 1364 pts |

AF, atrial fibrillation; NA, not applicable; NVAF, non-valvular atrial fibrillation; pts, patients.

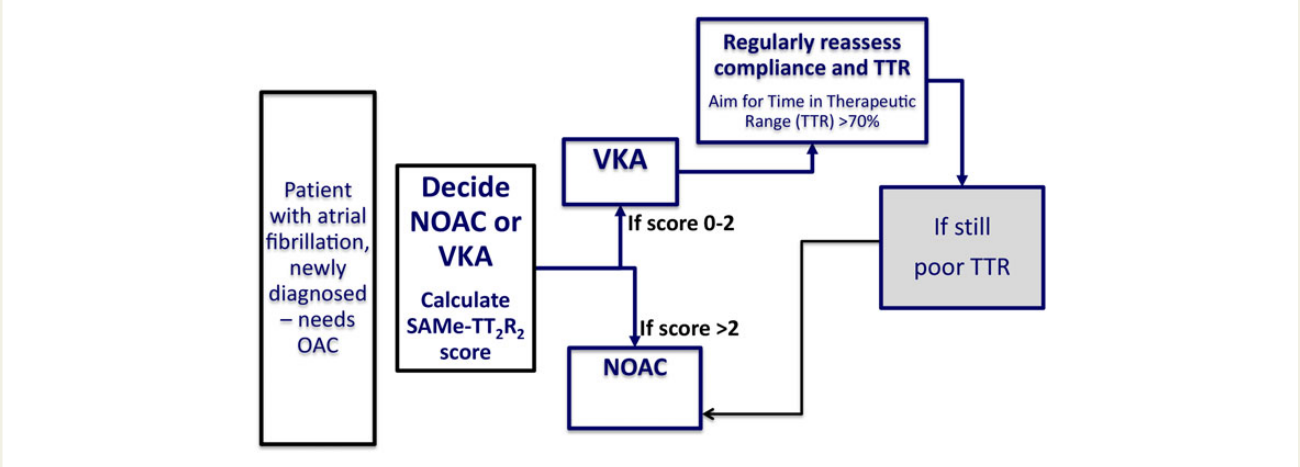


**Figure 1** Using the SAMe-$TT_2R_2$ score in a patient pathway. VKA, vitamin K antagonist; NOAC, non-VKA oral anticoagulant.

SAMe-$TT_2R_2$ score may offer that clinical utility for us, rather than relying on guesswork.

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