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Selection of Oral Anticoagulants in Atrial Fibrillation Patients Based on SAMe-TT2R2 Score

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SOUHRN

Při léčbě pacientů s fibrilací síní si lékař v klinické praxi musí vybrat mezi použitím antagonistů vitaminu K (VKA), jako je warfarin, a novými perorálními antikoagulancii. Podle observačních studií byly hodnoty mezinárodního normalizovaného poměru (international normalised ratio, INR) pacientů léčených podáváním VKA déle mimo terapeutické rozmezí (TTR < 60 %). Při použití běžných klinických kritérií může skórovací systém SAMe-TT2R2 pomoci zjistit, zda bude podávání VKA pro pacienta přínosné. Skóre SAMe-TT2R2 s hodnotami 0–1 by mělo ukazovat na přínos používání VKA, zatímco skóre 2 může svědčit o nepříznivé hodnotě TTR. Budeme zkoumat, jak spolehlivý je skórovací systém SAMe-TT2R2 při výběru perorálních antikoagulancií pro pacienty s fibrilací síní a zda se výzkum z poslední doby shoduje s našimi výsledky.

Keywords:
SAMe-TT2R2 score
Time in therapeutic range
Vitamin K antagonists

ABSTRACT

Clinicians must select between vitamin K antagonists (VKA) like warfarin and non-VKA oral anticoagulants for atrial fibrillation patients. According to observational studies, VKA patients have had international normalised ratio (INR) values outside the time in therapeutic range (TTR <60%) for a long period of time. Based on common clinical criteria, the SAMe-TT2R2 score may help evaluate whether a VKA will work for a patient. SAMe-TT2R2 scores of 0–1 should perform well on a VKA, whereas values of 2 may result in inadequate TTR. We will examine how consistent the SAMe-TT2R2 score is in selecting oral anticoagulants for atrial fibrillation patients and how recent research reinforces this.

Introduction

Most sustained arrhythmias are atrial fibrillations (AF). 1.5–2% of the industrialised world has AF, rising to 15% in people over 75. Preventing AF's fivefold stroke risk is crucial. Thus, after discussing the patient's values and preferences, antithrombotic medication should be individualised. Oral anticoagulation (OAC) prevents stroke in risky AF patients. Next, the physician must assess the danger of significant bleeding versus the benefit of minimising thromboembolism. For non-valvular AF thromboprophylaxis, simple risk stratification scores are routinely used.[1–3] AF patients' stroke risk was assessed using the CHA_2DS_2-VASc score. Compared to $CHADS_2$, this score covers more clinically significant stroke risk factors. For those with one stroke risk factor, OAC stroke prevention is next. Thus, male patients with CHA_2DS_2-VASc = 1 may balance stroke risk and bleeding risk with oral anticoagulants (Class IIa recommendation).[4]

The SAMe-TT2R2 Score

The SAMe-TT2R2 Score is a risk assessment tool used in the management of patients with AF who require anticoagulation therapy, specifically oral anticoagulants like warfarin or direct oral anticoagulants (DOACs). The SAMe-TT2R2 Score is used to evaluate the risk of poor an-

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ticoagulation control in AF patients who are prescribed warfarin. It helps determine the likelihood of achieving a time in therapeutic range (TTR) of less than 65%. TTR represents the proportion of time during which a patient's INR is within the target range.

The components of the SAMe-TT2R2 Score are as follows:

S: Sex (female gender),

A: Age (≥ 65 years),

M: Medical history (more than two comorbidities),

E: Ethnicity (non-Caucasian),

T: Treatment (interacting medications, e.g., amiodarone for rhythm control),

T: Tobacco use (smoking).

Each component is assigned one point, and the total score can range from 0 to 6. A higher score indicates a higher risk of poor anticoagulation control.

The SAMe-TT2R2 Score helps identify patients who may require closer monitoring or alternative anticoagulation strategies to optimize their treatment and reduce the risk of complications associated with AF, such as stroke. However, it's important to note that this score is primarily applicable to patients on warfarin therapy and may not have the same relevance for patients on DOACs. As always, healthcare professionals should consider the individual patient's characteristics and consult guidelines or expert recommendations for proper management. Our aim is to review how consistent the SAMe-TT2R2 score is in the selection of oral anticoagulants in patients with atrial fibrillation and to what extent new studies emphasise this.

Vitamin K antagonists therapy practicalities

Warfarin and non-vitamin K antagonist oral anticoagulants (NOACs) prevent strokes. Vitamin K antagonists (VKAs) cut stroke risk by 64% and all-cause mortality by 26% in AF. VKA is excellent for AF with a 2.0–3.0 INR. Dosage modification needs frequent coagulation monitoring. Medication interactions, vitamin K intake, hepatic impairment, compliance, and alcohol intake impact VKA dose response. Nonadherence is a primary reason VKA anticoagulation fails. VKAs increase bleeding, blood monitoring, and drug-drug or drug-food interactions. Non-adherence, medication cessation, and INR problems result. Ischemic stroke risk rises with anticoagulation discontinuation.[5–7]

The mismatch in stroke risk associated with AF has led to NOACs replacing VKAs in the prevention of thromboembolism and being similarly effective in the prevention of ischemic stroke with less intracranial bleeding and drug interactions. Compliance, health, and illness may quickly and permanently change anticoagulant control. INRs below 2.0 and above 3.5 promote ischemic episodes and cerebral haemorrhage.[8–11]

One comprehensive study found that VKA-treated individuals had INR levels well beyond the therapeutic range. Anticoagulation management quality is measured by time in therapeutic range (TTR). A higher TTR (>70%) is associated with fewer adverse events (thromboembolism, haemorrhage) in VKA patients. Compared to individuals with excellent anticoagulation management, those with TTR less than 35% had a fourfold higher mortality risk. Poor TTR (40%) increases stroke risk compared to untreated individuals. A high TTR reduces stroke and bleeding risks.[12,13]

Other methods define anticoagulation control quality. All clinical methods have benefits and downsides. The Rosendaal method estimates TTR by assuming linear changes between INR measurements and interpolating values not observed. The percentage of INRs within the therapeutic range (PINRR) method divides the total number of visits by the number with INR values between 2 and 3. PINRR still matches Rosendaal. Rosendaal TTR and PINNR differ despite their association ($r = 0.99$; $p = 0.001$). Few studies mention TTR and INR range percentages.[14,15]

Many trials demonstrate poor anticoagulation control. One multicenter European study randomised participants to a computer-generated dose or traditional administration. Computer-dosed patients had 63% TTR, whereas conventional patients had 53.2%. CALIFA, a countrywide, multicenter, observational, cross-sectional, retrospective investigation of AF patients having VKA at Spanish cardiology clinics, found that 47.3% had poorly managed anticoagulation and the mean TTR was 63.8%. NOACs may help experienced VKA patients with inadequate control.[16] NOAC's pharmacodynamic and pharmacokinetic properties imply more stable anticoagulation. NOACs have fewer food and pharmaceutical interactions than VKAs; therefore, laboratory anticoagulation monitoring is unnecessary.[17]

Clinical decision-making: NOAC vs VKA with excellent TTR?

Some healthcare systems need a 3- to 6-month "trial of VKA" or "warfarin stress test" to measure TTR. TTR determines NOAC reimbursement. Warfarin testing in AF patients may raise stroke risk during treatment.[18,19] Warfarin increased ischemic stroke risk by 71% in 30 days, peaking in the first few weeks, according to Azoulay et al.[20] INR fluctuations and poor TTR upon commencement may explain this early risk. Some physicians may have estimated whether a VKA would work for them. A Swedish registry indicated that 45% of patients did not have enough warfarin to last 80% of the risk period, and 16–21% quit within the first year, followed by 8–9% annually.[21,22]

INR control might improve. Understanding anticoagulant medicine improves INR values. Education may help atrial fibrillation patients manage anticoagulation. Self-monitoring improved TTR and thromboembolic events but not severe bleeding or death in an individual patient-data meta-analysis of self-management trials. Metaanalyses show that self-managing oral anticoagulants are equivalent to clinic treatment.[23]

Apostolakis et al.[24] internally validated the SAMe-TT2R2 score using data from the US-Canada Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study, a randomised, multicenter trial of 4060 patients with non-valvular AF at high risk of stroke or death. In 1089 warfarin-treated AF patients, Poli et al.[25] validated that the SAMe-TT2R2 score predicted a good

TTR (74%), a lower TTR (68%), no adverse events, and a decreased mean TTR (p <0.006).

In the Loire Valley Atrial Fibrillation Study, 8120 VKA-treated patients with labile INR had a significantly higher mean SAMe-TT2R2 score, which increased their risk of stroke or thromboembolism, severe bleeding, major haemorrhage, and death. Non-VKA users had no predicted SAMe-TT2R2 score.[26] Skov et al.[27] observed no significant correlation between SAMe-TT2R2 score and TTR in a limited (and perhaps underpowered) group of AF patients in a high-quality anticoagulation clinic (average TTR 76%). Gallego et al.[28] confirmed the SAMe-TT2R2 score in 972 consecutive AF patients on acenocoumarol instead of warfarin. High baseline SAMe-TT2R2 scores indicated poor anticoagulation management, which increased bleeding, adverse cardiovascular events, and death (p <0.001).

Another Spanish study by Abumuaileq et al.[29] retrospectively tested SAMe-TT2R2 in 911 outpatients with non-valvular AF. SAMe-TT2R2 was associated with major bleeding, thromboembolism complications, and death (p = 0.03), and the mean PINRR decreased from high to low scores (p = 0.001). PINRR replaced Rosendaal in this research. PINRR was fast and didn't need a computer, but it's not interchangeable with TTR. Roldán et al.[30] validated SAMe-TT2R2 in "real-world" VKA-initiated anticoagulation-naive patients. SAMe-TT2R2 scores <2 were linked with increased mean TTR (p = 0.001). SAMe-TT2R2 score 2 had a 2.10 odds ratio for low TTR (95% CI 1.44–3.06, p <0.001). Ruiz-Ortiz et al.[31] confirmed SAMe-TT2R2 in CALIFA. VKA preceded inclusion. 1056 individuals with scores 0–1 showed substantially higher mean TTR values than those with 0–2 and >2. The SAMe-TT2R2 score may also identify labile INRs based on various criteria (e.g., TTR <65%; 2 INR values higher than 5 or 1 higher than 8 in the previous 6 months; 2 INR values less than 1.5 in the last 6 months; PINRR <65%).

Realistic concerns

SAMe-TT2R2 was originally developed to predict severe TTR outliers in anticoagulated patients; however, recent research has shown that it also predicts labile INR and its implications. Thromboembolism, death, bleeding, and cardiovascular events are examples. In non-VKA patients, the score was unpredictive. Clinical risk ratings typically have a c-statistic of 0.6–0.7. $CHADS_2$ and CHA_2DS_2-VASc have comparable c-statistics for AF stroke risk classification.[32]

Demographics, study settings, and VKA types may explain these disparities. SAMe-TT2R2 has only been validated in Caucasian cohorts; hence, other ethnic groups must be tested. Individual TTR ranges from 50% in Eastern Europe to 63% in Asia and 64% in Western Europe, Canada, and the US. Women have weaker SAMe-TT2R2. VKAs protect women against stroke, while sex-related variations cause more. Women, especially those over 75, had a greater stroke risk than men, independent of risk profile or warfarin usage, according to many studies. Research shows women adhere to warfarin better than men. In younger women, menstrual hormones might impact anticoagulation, and small bleeds can halt therapy. SAMe-TT2R2 >2 only weakened anticoagulant control in younger females.[33–36]

NOACs are safer and more effective for women than men, according to RE-LY, ARISTOTLE, and ROCKETAF.[37] Non-Caucasians score 2 – why? Apostolakis et al.[25] observed that race and socioeconomic status may alter TTR. Westerners had more INRs of 2.0–3.0 than Asians. Asian warfarin-treated AF patients had a 4.06 HR for cerebral haemorrhage compared to whites in a retrospective cohort study. Asians bled more than non-Asians in RE-LY, ROCKET-AF, and ARISTOTLE. Asian RE-LY participants had a mean TTR of 54.5% and non-Asians 66.2%, with 35.4% INR <2.0 (non-Asians 19.8%). SAMe-TT2R2 contains race since it affects anticoagulation.[38]

Patients should be assessed for effective anticoagulation therapy or NOAC usage using SAMe-TT2R2. Adding alcohol excess, liver or renal disorders, etc., may increase the SAMe-TT2R2 score's predictive value. A patient with a decent TTR may benefit from a VKA based on the SAMe-TT2R2 score. If a strong TTR is improbable (SAMe-TT2R2 score >2), start the patient on a NOAC or provide education, clinical testing, and follow-up. This treatment requires prospective clinical studies.

Recent studies

Nonvalvular AF (NVAF) and coronary heart disease (CHD) patients with the ABC (age, biomarkers, clinical history) bleeding score and SAMe-TT2R2 score may bleed after anticoagulation. In NVAF and CHD patients, the SAMe--TT2R2 score may need to be raised to 4 or 5, and the ABC bleeding score predicts bleeding better.[39] In warfarin-treated NVAF patients, SAMe-TT2R2 alone predicted poor TTR. Low C-statistics may limit score discrimination.[40] The SAMe-TT2R2 score predicted poor INR control in VKA-treated VTE patients but was not predictive. The score's clinical decision-making value requires more investigation.[41]

CHA_2DS_2-VASc and SAMe-TT2R2 scores predicted 1-year atrial fibrillation on vitamin K antagonists after radiofrequency catheter ablation (RFCA). At least 3 CHA_2DS_2-VASc and 5 SAMe-TT2R2 levels indicated atrial fibrillation recurrence.[42] Digoxin is widely used to treat heart failure and AF, despite the therapeutic range's (oTR) mortality concerns. In this study, modified SAMe-TT2R2 predicted the oTR. This score may help doctors identify digoxin-responsive patients.[43] SAMe-TT2R2 could not predict anticoagulation control in Qatari warfarin-treated venous thromboembolism (VTE) patients. Other clinical factors and scores may enhance anticoagulant control prediction.[44] In another study, the SAMe-TT2R2 score predicted poor anticoagulation in Qatari patients.[45]

SAMe-TT2R2 >3 VKA patients had more adverse events, haemorrhage, and thrombosis. Trial TTR was predicted badly by the score.[46] SAMe-TT2R2 identified warfarin-resistant Australians without race. Australian clinicians may use the SAMe-TT2R2 score to identify patients who need additional warfarin therapy, such as a warfarin care programme (WCP).[47] SAMe-TT2R2 predicts a low TTR, but only slightly. Its clinical impact on patients is too little.[48] Hwang et al.[49] imply the SAMe-TT2R2 score predicts

Table 1 – The main topic points of recent studies

Reference no.	Authors	Subjects	Main theme
5	Gallagher et al.	Patients with atrial fibrillation	Anticoagulation management reduced stroke risk.
20	Azoulay et al.	Patients with atrial fibrillation	Warfarin increased ischemic stroke risk by 71% in 30 days, peaking in the first few weeks.
22	Skeppholm et al.	Patients with atrial fibrillation	Prescription data may compare group warfarin adherence to new oral anticoagulants. A large warfarin-treated atrial fibrillation sample showed low adherence, requiring improvements.
23	Apostolakis et al.	Patients with atrial fibrillation	Oral anticoagulant self-management was comparable to clinic management. Self-management reduced significant consequences and small haemorrhages.
39	Du et al.	Patients with nonvalvular atrial fibrillation	Nonvalvular AF (NVAF) and coronary heart disease (CHD) patients with the ABC (age, biomarkers, clinical history) bleeding score and SAMe-TT2R2 score may bleed after anticoagulation.
40	Krittayaphong et al.	Thai population with atrial fibrillation	In warfarin-treated NVAF patients, SAMe-TT2R2 alone predicted poor TTR. Low C-statistics may limit score discrimination.
41	Del-Toro-Cervera et al.	Patients with venous thromboembolism	The SAMe-TT2R2 score predicted poor INR control in VKA-treated VTE patients but was not predictive.
42	Zhao et al.	Nonvalvular atrial fibrillation patients	CHA_2DS_2-VASc and SAMe-TT2R2 scores predicted 1-year atrial fibrillation on vitamin K antagonists after radiofrequency catheter ablation (RFCA). At least 3 CHA_2DS_2-VASc and 5 SAMe-TT2R2 levels indicated atrial fibrillation recurrence.
43	Karataş et al.	Patients who were under digoxin treatment.	Digoxin is widely used to treat heart failure and AF, despite the therapeutic range's (oTR) mortality concerns. In this study, modified SAMe-TT2R2 predicted the oTR. This score may help doctors identify digoxin-responsive patients.
44	Alhmoud et al.	Patients with venous thromboembolism	SAMe-TT2R2 could not predict anticoagulation control in Qatari warfarin-treated venous thromboembolism (VTE) patients. Other clinical factors and scores may enhance anticoagulant control prediction.
45	Elewa et al.	Qatari patients treated with warfarin	The SAMe-TT2R2 score predicted poor anticoagulation in Qatari patients.
46	Incomenoy et al.	Patients on vitamin K antagonists	SAMe-TT2R2 >3 VKA patients had more adverse events, haemorrhage, and thrombosis. Trial TTR was predicted badly by the score.
47	Bernaitis et al.	Australian population with atrial fibrillation	SAMe-TT2R2 identified warfarin-resistant Australians without race. Australian clinicians may use the SAMe-TT2R2 score to identify patients who need additional warfarin therapy, such as a warfarin care programme.
48	van Miert et al.	16 studies (meta-analysis)	SAMe-TT2R2 predicts a low TTR, but only slightly.
49	Hwang et al.	Patients receiving chronic anticoagulation	The SAMe-TT2R2 score predicts extended-interval warfarin follow-up success, but additional study is required.

extended-interval warfarin follow-up success, but additional study is required. The main topic points of recent studies are shown in **Table 1**.

Conclusion

SAMe-TT2R2 may help identify individuals at high risk of poor anticoagulation control and enhance their anticoagulation medication. This score should be done before commencing anticoagulant treatment to identify clinical factors linked to poor INR control that physicians may address (e.g., interacting drugs) or monitor more often.

Conflict of interest
The authors declare that there is no conflict of interest regarding the publication of this paper.

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Ethical statement
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References

1. Camm AJ, Lip GYH, De Caterina R, et al. 2012 focused update of the ESC guidelines for the management of atrial fibrillation: an update of the 2010 ESC guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012;33:2719–2747.
2. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:2246–2280.
3. Olesen JB, Torp-Pedersen C. Stroke risk in atrial fibrillation: do we anticoagulate CHADS2 or CHA2DS2-VASc ≥1, or higher? Thromb Haemost 2015;113:1165–1169.
4. Senoo K, Lau YC, Lip GY. Updated NICE guideline: management of atrial fibrillation. Expert Rev Cardiovasc Ther 2014;12:1037–1040.
5. Gallagher AM, Setakis E, Plumb JM, et al. Risks of stroke and mortality associated with suboptimal anticoagulation in atrial fibrillation patients. Thromb Haemost 2011;106:968–977.
6. De Caterina R, Husted S, Wallentin L, et al. Vitamin K antagonists in heart disease: current status and perspectives (Section III). Position paper of the ESC Group on Thrombosis – Task Force on Anticoagulants in Heart Disease. Thromb Haemost 2013;110:1087–1107.
7. Sanfélix-Gimeno G, Rodríguez-Bernal CL, Hurtado I, et al. Adherence to oral anticoagulants in patients with atrial fibrillation-a population-based retrospective cohort study linking health information systems in the Valencia region, Spain: a study protocol. BMJ Open 2015;5:e007613.
8. Jurcuț R, Militaru S, Geavlete O, et al. Predictive factors for obtaining a correct therapeutic range using antivitamin K anticoagulants: a tertiary center experience of patient adherence to anticoagulant therapy. Patient Prefer Adherence 2015;9:1271–1278.
9. Nielsen PB, Chao TF. The risks of risk scores for stroke risk assessment in atrial fibrillation. Thromb Haemost 2015;113:1170–1173.
10. Eikelboom JW, Weitz JI. "Real world" use of non-vitamin K antagonist oral anticoagulants (NOACs): lessons from the Dresden NOAC registry. Thromb Haemost 2015;113:1159–1161.
11. Fauchier L, Poli D, Olshansky B. The SAMe-TT2R2 score and quality of anticoagulation in AF: can we predict which patient benefits from anticoagulation? Thromb Haemost 2015;114:657–659.
12. Van Den Ham HA, Klungel OH, Leufkens HGM, et al. The patterns of anticoagulation control and the risk of stroke, bleeding and mortality in patients with non-valvular atrial fibrillation. J Thromb Haemost 2013;11:107–115.
13. Sjögren V, Grzymala-Lubanski B, Renlund H, et al. Safety and efficacy of well managed warfarin. A report from the Swedish quality register Auricula. Thromb Haemost 2015;113:1370–1377.
14. Wan Y, Heneghan C, Perera R, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. Circ Cardiovasc Qual Outcomes 2008;1:84–91.
15. Fauchier L, Angoulvant D, Lip GYH. The SAMe-TT2R2 score and quality of anticoagulation in atrial fibrillation: a simple aid to decision-making on who is suitable (or not) for vitamin K antagonists. Europace 2015;17:671–673.
16. Anguita Sánchez M, Bertomeu Martínez V, Cequier Fillat Á, CALIFA study researchers. Quality of vitamin K antagonist anticoagulation in Spain: prevalence of poor control and associated factors. Rev Esp Cardiol (Engl Ed) 2015;68:761–768.
17. Mani H, Lindhoff-Last E. New oral anticoagulants in patients with nonvalvular atrial fibrillation: a review of pharmacokinetics, safety, efficacy, quality of life, and cost effectiveness. Drug Des Devel Ther 2014;8:789–798.
18. Lau YC, Lip GYH. Which drug should we use for stroke prevention in atrial fibrillation? Curr Opin Cardiol 2014;29:293–300.
19. Proietti M, Lip GYH. Simple decision making between a vitamin K antagonist and non-vitamin K antagonist oral anticoagulant (NOACs): using the SAMe-TT2R2 score. Eur Heart J Cardiovasc Pharmacother 2015;1:150–152.
20. Azoulay L, Dell'Aniello S, Simon TA, et al. Initiation of warfarin in patients with atrial fibrillation: early effects on ischaemic strokes. Eur Heart J 2014;35:1881–1887.
21. Lip GYH. Stroke prevention in atrial fibrillation: changing concepts. Eur Heart J Cardiovasc Pharmacother. 2015;1:76–79.
22. Skeppholm M, Friberg L. Adherence to warfarin treatment among patients with atrial fibrillation. Clin Res Cardiol 2014;103:998–1005.
23. Menéndez-Jándula B, Souto JC, Oliver A, et al. Comparing self-management of oral anticoagulant therapy with clinic management: a randomized trial. Ann Intern Med 2005;142:1–10.
24. Apostolakis S, Sullivan RM, Olshansky B, et al. Factors affecting quality of anticoagulation control among patients with atrial fibrillation on warfarin: the SAMeTT$_2$R$_2$ score. Chest 2013;144:1555–1563.
25. Poli D, Antonucci E, Testa S, et al. A prospective validation of the SAME-TT2R2 score: how to identify atrial fibrillation patients who will have good anticoagulation control on warfarin. Intern Emerg Med 2014;9:443–447.
26. Lip GYH, Haguenoer K, Saint-Etienne C, et al. Relationship of the SAMe-TT$_2$R$_2$ score to poor-quality anticoagulation, stroke, clinically relevant bleeding, and mortality in patients with atrial fibrillation. Chest 2014;146:719–726.
27. Skov J, Bladbjerg E-M, Bor MV, et al. SAMeTT(2)R(2) does not predict time in therapeutic range of the international normalized ratio in patients attending a high-quality anticoagulation clinic. Chest 2014;145:187–188.
28. Gallego P, Roldán V, Marin F, et al. SAMe-TT2R2 score, time in therapeutic range, and outcomes in anticoagulated patients with atrial fibrillation. Am J Med 2014;127:1083–1088
29. Abumuaileq RR-Y, Abu-Assi E, Raposeiras-Roubin S, et al. Evaluation of SAMe-TT2R2 risk score for predicting the quality of anticoagulation control in a real-world cohort of patients with non-valvular atrial fibrillation on vitamin-K antagonists. Europace 2015;17:711–717.
30. Roldán V, Cancio S, Gálvez J, et al. The SAMe-TT2R2 score predicts poor anticoagulation control in AF patients: a prospective "real-world" inception cohort study. Am J Med 2015;128:1237–1243.
31. Ruiz-Ortiz M, Bertomeu V, Cequier Á, et al. Validation of the SAMe-TT2R2 score in a nationwide population of nonvalvular atrial fibrillation patients on vitamin K antagonists. Thromb Haemost 2015;114:695–701.
32. Lip GYH, Lane DA. Stroke prevention in atrial fibrillation: a systematic review. Jama 2015;313:1950–1962.
33. Singer DE, Hellkamp AS, Piccini JP, et al. Impact of global geographic region on time in therapeutic range on warfarin anticoagulant therapy: data from the ROCKET AF clinical trial. J Am Heart Assoc 2013;2:e000067.
34. Apostolakis SZ, Konstantinides SV. Gender and the risk of stroke in atrial fibrillation: impact of old and new anticoagulation regimens. Clin Res Cardiol Suppl 2013;1:38–45.
35. Avgil Tsadok M, Jackevicius CA, Rahme E, et al. Sex differences in stroke risk among older patients with recently diagnosed atrial fibrillation. JAMA 2012;307:1952–1958.
36. Tomita H, Kadokami T, Momii H, et al. Patient factors against stable control of warfarin therapy for Japanese non-valvular atrial fibrillation patients. Thromb Res 2013;132:537–542.
37. Vallurupalli S, Deshmukh A, Paydak H. Gender based differences in benefit from novel oral anticoagulant drugs compared to warfarin in atrial fibrillation: an analysis of published studies. J Am Coll Cardiol 2014;63(12).
38. Wang KL, Chiang CE. Optimal international normalized ratio for atrial fibrillation in Asians and Japanese: do we really know? Circ J 2013;77:2242–2243.
39. Du M, Li F, Zhang A, et al. Evaluation of ABC Bleeding Score and SAMe-TT2R2 Score on the Risk of Bleeding after Anticoagulation in Patients with Nonvalvular Atrial Fibrillation Complicated with Coronary Heart Disease. Contrast Media Mol Imaging 2022;2022:6982753.

40. Krittayaphong R, Winijkul A, Pirapatdit A, et al. SAMe-TT2R2 score for prediction of suboptimal time in therapeutic range in a Thai population with atrial fibrillation. Singapore Med J 2020;61:641–646.
41. Del-Toro-Cervera J, Demelo-Rodriguez P, Galeano-Valle F, et al. Evaluation of the SAMe-TT2R2 score to predict the quality of anticoagulation control in patients with venous thromboembolism treated with vitamin K antagonists: Findings from the RIETE registry. Thromb Res 2020;194:178–182.
42. Zhao J, Zhou D, Chen M, et al. CHA2DS2-VASc and SAMe-TT2R2 scores as predictors of recurrence for nonvalvular atrial fibrillation patients on vitamin K antagonists after radiofrequency catheter ablation. J Cardiovasc Med (Hagerstown) 2020;21:200–208.
43. Karataş MB, Çanga Y, Yelgeç NS, et al. Modified SAMe-TT2R2 score for predicting the therapeutic range of digoxin. Herz 2021;46:359–366.
44. Alhmoud EN, Elewa H, Abdul Gelil MS, et al. Evaluation of the Validity of SAMe-TT2R2 Score in a Cohort of Venous Thromboembolism Patients Treated With Warfarin. Clin Appl Thromb Hemost 2020;26:1076029620945039.
45. Elewa H, Qurishi I, Abouelhassan R, et al. Effect of SAMe-TT2R2 score and genetic polymorphism on the quality of anticoagulation control in Qatari patients treated with warfarin. J Thromb Thrombolysis 2020;49:659–666.
46. Incomenoy S, Saokaew S, Poonchuay N. SAMe-TT_2R_2 to Predict Clinical Outcomes and Time in Therapeutic Range in Patients on Vitamin K Antagonists: A Systematic Review and Meta-Analysis. Ann Pharmacother 2024;58:126–139.
47. Bernaitis N, Clark G, Kohja S, et al. The SAMe-TT2R2 Score Predicts Warfarin Control in an Australian Population with Atrial Fibrillation. J Clin Med 2019;8:882.
48. van Miert JHA, Bos S, Veeger NJGM, et al. Clinical usefulness of the SAMe-TT2R2 score: A systematic review and simulation meta-analysis. PLoS One 2018;13:e0194208.
49. Hwang AY, Carris NW, Dietrich EA, et al. Evaluation of SAMe-TT2R2 Score on Predicting Success With Extended-Interval Warfarin Monitoring. Ann Pharmacother 2018;52:1085–1090.