

# Use of SAME-TT<sub>2</sub>R<sub>2</sub> Score to Predict the Quality of Anticoagulation Control in Patients with Atrial Fibrillation Receiving Warfarin in Thailand

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**Objective:** To predict the quality of anticoagulation control in patients with atrial fibrillation (AF) receiving warfarin in Thailand.

**Materials and Methods:** The present study retrospectively recruited Thai AF patients receiving warfarin for three months or longer between June 2012 and December 2017 in Central Chest Institute of Thailand. The patients were classified into those with SAME-TT<sub>2</sub>R<sub>2</sub> of 2 or less, and 3 or more. The Chi-square test or Fisher's exact test was used to compare the proportion of the patients with poor time in therapeutic range (TTR) between the two groups of SAME-TT<sub>2</sub>R<sub>2</sub> score. The discrimination performance of SAME-TT<sub>2</sub>R<sub>2</sub> score was demonstrated with c-statistics.

**Results:** Ninety AF patients were enrolled. An average age was 69.89±10.04 years. Most patients were persistent AF. An average CHA<sub>2</sub>DS<sub>2</sub>-VASc, SAME-TT<sub>2</sub>R<sub>2</sub>, and HAS-BLED score were 3.68±1.51, 3.26±0.88, and 1.98±0.85, respectively. The present study showed the increased proportion of AF patients with poor TTR with higher SAME-TT<sub>2</sub>R<sub>2</sub> score. The AF patients with SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more had a larger proportion of patients with poor TTR than those with SAME-TT<sub>2</sub>R<sub>2</sub> score of 2 or less with statistical significance when TTR was below 70% (p=0.03) and 65% (p=0.04), respectively. The discrimination performance of SAME-TT<sub>2</sub>R<sub>2</sub> score was demonstrated with c-statistics of 0.60, 0.59, and 0.55 when TTR was below 70%, 65% and 60%, respectively.

**Conclusion:** Thai AF patients receiving warfarin had a larger proportion of patients with poor TTR when the SAME-TT<sub>2</sub>R<sub>2</sub> score was higher. The score of 3 or more could predict poor quality of anticoagulation control in those patients.

**Keywords:** Time in therapeutic range, Poor quality of anticoagulation control, Warfarin, SAME-TT<sub>2</sub>R<sub>2</sub>, Labile INR

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Stroke prevention in patients with atrial fibrillation (AF) is of paramount importance in clinical practice because acute cardioembolic stroke is a devastating disease in those patients. To date, oral anticoagulants are recommended in AF patients with non-sex CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1 or more (score of 1 or more in a male or 2 or more in a female)<sup>(1-3)</sup>. Poor time in therapeutic range (TTR)

is a common problem in those patients receiving warfarin in Thailand. Previous trials by Methavigul et al showed the percentage of patient-time spent within international normalized ratio (INR) 2 to 3 were 46.22%<sup>(4)</sup>.

Apostolakis et al proposed using SAME-TT<sub>2</sub>R<sub>2</sub> [Sex female, Age <60 years, Medical history (more than two comorbidities), Treatment (interacting drugs, e.g., amiodarone for rhythm control), Tobacco use (doubled), Race (doubled)] score to predict poor TTR<sup>(5)</sup>. Several clinical trials have demonstrated the score of 3 or more could predict poor anticoagulation control<sup>(6-9)</sup>.

However, data about using SAME-TT<sub>2</sub>R<sub>2</sub> score in Thai AF patients are scarce and limited by small sample size<sup>(10)</sup>. The present study was conducted to predict the quality of anticoagulation control in Thai AF patients receiving warfarin.

## Materials and Methods

The present study retrospectively recruited Thai

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**Table 1.** Baseline characteristics of the patients

Demographic data	Total n=90 n (%)
Age (years); mean±SD	69.89±10.04
Male gender	52 (57.78)
Paroxysmal AF	23 (25.56)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score; mean±SD	3.68±1.51
SAMe-TT <sub>2</sub> R <sub>2</sub> score; mean±SD	3.26±0.88
HAS-BLED score; mean±SD	1.98±0.85
LVEF (%); mean±SD	54.54±18.26
Time in therapeutic range (%); mean±SD	53.17±25.36
eGFR (ml/minute/1.73m <sup>2</sup> ); mean±SD	68.55±18.55
<b>Medical history</b>	
Diabetes mellitus	23 (25.56)
Hypertension	73 (81.11)
Hypercholesterolemia	72 (80.00)
Coronary artery disease	29 (32.22)
Peripheral artery disease	1 (1.11)
Valvular heart disease	14 (15.56)
Chronic kidney disease	26 (28.89)
History of previous ischemic stroke or TIA	17 (18.89)
History of heart failure	31 (34.44)
History of liver disease	0 (0.00)
History of pulmonary disease	4 (4.44)
History of smoking within 2 years	10 (11.11)
<b>Medications</b>	
Beta-blockers	70 (77.78)
Non-dihydropyridine CCB	5 (5.56)
Digoxin	25 (27.78)
Amiodarone	4 (8.89)
Flecainide	1 (1.11)
Warfarin	90 (100)
Aspirin	8 (8.89)
Clopidogrel	12 (13.33)

SD=standard deviation; n=numbers; AF=atrial fibrillation; TIA=transient ischemic attack; LVEF=left ventricular ejection fraction; eGFR=estimated glomerular filtration rate; ml=millimeter; CCB=calcium channel blockers

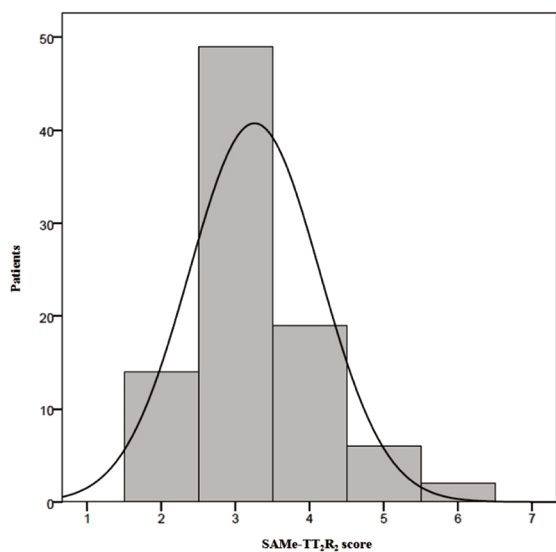
AF patients receiving warfarin for three months or more between June 2012 and December 2017 in Central Chest Institute of Thailand. Those patients aged below 18 years, duration of warfarin usage of less than one year, each INR during follow-up visit lasting more than six months, hospitalization during study, warfarin interruption from surgery, intervention or any causes, those with prosthetic heart valve,

platelet count below 100,000/mm<sup>3</sup>, myeloproliferative disorders including essential thrombocythemia, chronic myeloid leukemia, polycythemia vera, agnogenic myeloid metaplasia, hyperviscosity syndrome, or pregnancy were excluded. The SAMe-TT<sub>2</sub>R<sub>2</sub> score included Sex female, Age less than 60 years, Medical history of more than two of the following comorbidities: hypertension, diabetes, coronary artery disease or myocardial infarction, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, hepatic or renal disease, Treatment with interacting drugs such as amiodarone for rhythm control, Tobacco use (doubled), and non-Caucasian Race (doubled). The quality of anticoagulation control was measured by TTR calculating by using Rosendaal method<sup>(11)</sup>. The poor TTR was defined as the INR level of less than 60%, 65%, or 70% of follow-up period<sup>(12)</sup>. The patients were classified into those with SAMe-TT<sub>2</sub>R<sub>2</sub> of 2 or less, and 3 or more. The study protocol was approved by the Institutional Review Board. The present study complied with the Declaration of Helsinki.

The author determined 0.05 for type I error, 0.10 for type II error with 90% power and estimated the proportions of poor TTR in AF patients with SAMe-TT<sub>2</sub>R<sub>2</sub> of 2 or less and 3 or more were 0.25 and 0.78, respectively<sup>(10)</sup>. The ratio of SAMe-TT<sub>2</sub>R<sub>2</sub> of 2 or less to those of 3 or more was 0.11. A sample size of 90 patients was calculated to compare populations of the two groups by Chi-square test. The demographic and clinical data were interpreted by using descriptive statistics. The categorical data were presented as frequency and percentage. The continuous variables were presented as mean ± standard deviation (SD). The Chi-square test or Fisher's exact test was used to compare the proportion of the patients with poor TTR between the two groups of SAMe-TT<sub>2</sub>R<sub>2</sub> score. The discrimination performance of SAMe-TT<sub>2</sub>R<sub>2</sub> score was demonstrated with c-statistics. A p-value of 0.05 or less was considered statistical significance.

## Results

Ninety AF patients were enrolled. An average age was 69.89±10.04 years. Most patients were persistent AF. The average CHA<sub>2</sub>DS<sub>2</sub>-VASc, SAMe-TT<sub>2</sub>R<sub>2</sub>, and HAS-BLED score were 3.68±1.51, 3.26±0.88, and 1.98±0.85, respectively. Most patients had hypertension and hypercholesterolemia. Nearly one-fifth of those had the history of ischemic stroke or transient ischemic attack (TIA). A one-third of them experienced heart failure. The baseline characteristics of the patients are shown in Table 1.



**Figure 1.** The distribution of Thai AF patients according to SAME-TT<sub>2</sub>R<sub>2</sub> score.

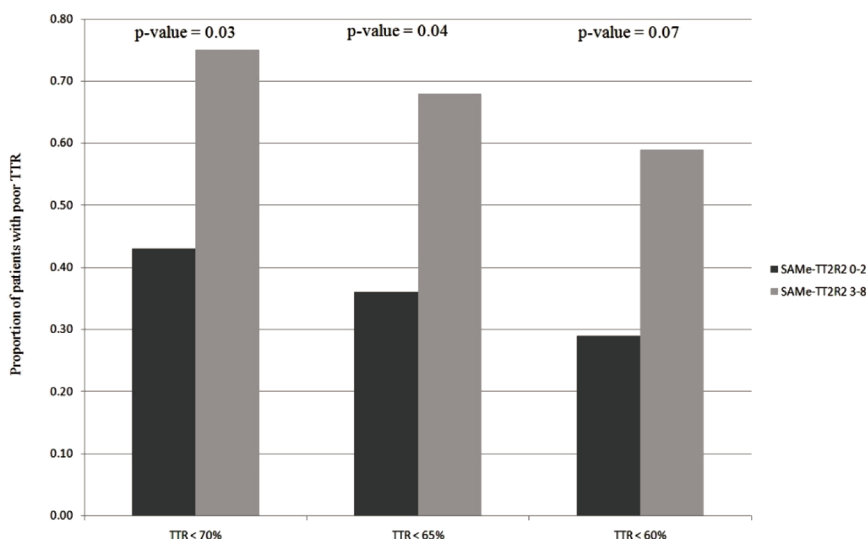
The present study showed a larger proportion of AF patients with poor TTR following an increased SAME-TT<sub>2</sub>R<sub>2</sub> score and the distribution of those patients according to SAME-TT<sub>2</sub>R<sub>2</sub> score is shown in Figure 1. The patients with SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more had a larger proportion of patients with poor TTR than those with SAME-TT<sub>2</sub>R<sub>2</sub> score of 2 or less with statistical significance when TTR was below 70% ( $p=0.03$ ) and 65% ( $p=0.04$ ), respectively as shown in Figure 2. The discrimination performance of SAME-TT<sub>2</sub>R<sub>2</sub> score was demonstrated with c-statistics

of 0.60, 0.59, and 0.55 when TTR was below 70%, 65%, and 60%, respectively.

## Discussion

The present study demonstrated that a SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more increased the risk of poor TTR in Thai AF patients. Previous trial had shown the SAME-TT<sub>2</sub>R<sub>2</sub> score of 2 or more could predict the quality of anticoagulant control<sup>(5,13)</sup>. However, later trials have shown the SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more was better predictor in AF patients with poor TTR<sup>(6-9,14)</sup>. According to a 2017 consensus of the Asia Pacific Heart Rhythm Society (APHRS) on stroke prevention in AF, non-vitamin K antagonist oral anticoagulant (NOAC) was recommended in AF patients with the SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more because they were unlikely to achieve a good TTR by taking vitamin K antagonist (VKA)<sup>(15)</sup>. The present trial had the same results compared with the previous trials and showed that Thai AF patients could use SAME-TT<sub>2</sub>R<sub>2</sub> score to predict the quality of anticoagulation control as well.

The discrimination performance of SAME-TT<sub>2</sub>R<sub>2</sub> score was demonstrated by c-statistics between 0.55 to 0.60 depending on definition of poor TTR, which was lower than a previous trial by Apostolakis et al<sup>(5)</sup>. Those trial showed that the SAME-TT<sub>2</sub>R<sub>2</sub> score had good discrimination performance (c-statistics 0.70). Moreover, a systematic review suggested that the SAME-TT<sub>2</sub>R<sub>2</sub> score could predict the quality of anticoagulation control in AF patients receiving VKA with c-statistics ranging from 0.56 to 0.72<sup>(16)</sup>.



**Figure 2.** The proportion of Thai AF patients with poor TTR according to SAME-TT<sub>2</sub>R<sub>2</sub> categories.

Each previous trials had a different discrimination performance including the present trial because the SAME-TT<sub>2</sub>R<sub>2</sub> score was a clinical prediction tool that does not include some risk predictors of poor TTR such as the elderly patients, alcohol abuse, concomitant antiplatelet drugs etc. Additionally, good TTR is dependent on each physician. The physician inertia is a common problem because they do not concern about warfarin adjustment for good TTR and duration of follow-up visit is another problem. Long duration of follow-up visit has more risk of poor TTR than short period of follow-up visit. Therefore, the use of SAME-TT<sub>2</sub>R<sub>2</sub> score in clinical practice should be accompanied with other clinical profile of each patient.

The present study had some limitations. First, the present study had small sample size. However, it has shown that a SAME-TT<sub>2</sub>R<sub>2</sub> score of 3 or more increases the risk of poor TTR in Thai AF patients with statistical significance. Second, the present study was a retrospective study, so missing data or selection bias cannot be excluded. However, the preliminary evidence demonstrated that those scores can be used in Thai AF patients.

## Conclusion

Thai AF patients receiving warfarin had a larger proportion of patients with poor TTR when the SAME-TT<sub>2</sub>R<sub>2</sub> score is higher. Those score of 3 or more could predict poor quality of anticoagulation control in those patients.

## What is already known on this topic?

The SAME-TT<sub>2</sub>R<sub>2</sub> score can be used to predict the poor TTR in AF patients receiving warfarin.

## What this study adds?

The SAME-TT<sub>2</sub>R<sub>2</sub> score can use to predict the poor TTR in the Thai AF patients receiving warfarin, which is similar to the Caucasian population.

## Conflicts of interest

The author declares no conflict of interest.

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