Original Article

SAMe-TT_2R_2 Score for Prediction of Anticoagulation Control in Thai Patients with Non-Valvular Atrial Fibrillation

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Background: The quality of anticoagulation control is an important determination of thromboembolism and bleeding in patients with non-valvular atrial fibrillation. Previous trials have shown that SAMe-TT_2R_2 score could be used for prediction of anticoagulation control.

Objective: To predict labile international normalized ratio (INR) by SAMe-TT_2R_2 score in Thai patients with non-valvular atrial fibrillation.

Materials and Methods: The author retrospectively studied patients with non-valvularatrial fibrillation at Pranangklao Hospital between January 2019 and October 2020.

Results: One hundred thirty patients were enrolled. The average ages of the patients were 67.5±10.2 years. The average SAMe-TT_2R_2 scores were 3.2±0.8 and the average CHA_2DS_2-VASc score was 3.3±1.4. Most patients had hypertension and dyslipidemia. Most patients were prescribed beta-blockers. Most patients had time in therapeutic range (TTR) lower than 65. The present study has shown that patients with SAMe-TT_2R_2 score of 3 or more has also had high proportion of labile INR with statical significance. The sensitivity, specificity, positive predictive value, and negative predictive value of different cut-offs of SAMe-TT_2R_2 score greater than 2 and SAMe-TT_2R_2 score when excluding race showed improvement of the sensitivity and specificity for prediction of labile INR.

Conclusion: Labile INR was predicted by SAMe-TT_2R_2 score and the sensitivity and specificity increased in SAMe-TT_2R_2 score when excluding race.

Keywords: SAMe-TT_2R_2 score; Non-valvular atrial fibrillation; Anticoagulation control

Received 5 February 2021 | Revised 16 April 2021 | Accepted 20 April 2021

J Med Assoc Thai 2021;104(6):959-63

Website: http://www.jmatonline.com

Atrial fibrillation is a common disease in cardiac clinics[1]. It could be found in two to four percent of adult patients[2-4]. Care must be correctly performed with the stimulus factors, including pulse rate, pulse rhythms, and anticoagulants to prevent thromboembolic stroke[5].

At present, warfarin is widely used in the prevention of first and repeated strokes in patients with atrial fibrillation based on the CHA_2DS_2VASc score with greater than or equal to 1[6-8].

The international normalized ratio (INR) should be 2 to 3 during the treatment program and should not fluctuate[9,10].

Patients taking Warfarin could be followed up with level of INR in long-term treatment[11].

When the time in therapeutic range (TTR) is less than 60%, it results in the severe bleeding and higher mortality. However, when TTR level during the treatment duration is more than 75%, the bleeding severity and mortality rate is reduced significantly[12].

In patients with atrial fibrillation, warfarin should be considered for stroke prevention[13] using the following table.

1. C=congestive heart failure (1 point)
2. H=hypertension (1 point)
3. A=age older than 75 years (2 points)
4. D=diabetes mellitus (1 point)
5. S=stroke (2 points)
6. V=vascular disease (1 point)
7. A=age 65 to 74 years (1 point)
8. Sc=female gender (1 point)

SAMe-TT_2R_2 score[14] is a tool to predict INR level control in patients who begin with Warfarin. According to the study, the SAMe-TT_2R_2 scores are

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How to cite this article:

Leedumrongwattanakul A. SAMe-TT_2R_2 Score for Prediction of Anticoagulation Control in Thai Patients with Non-Valvular Atrial Fibrillation. J Med Assoc Thai 2021;104:959-63.

doi.org/10.35755/jmedassocthai.2021.06.12415

calculated as follows:

1. S=female gender (1 point)
2. A=age younger than 60 years (1 point)
3. Me=medical history consisting of at least two conditions, diabetes mellitus, hypertension, heart failure, coronary artery disease, peripheral arterial disease, previous stroke, pulmonary disease, and hepatic or renal disease (1 point)
4. T=treatment with interacting drugs such as amiodarone, non-steroidal anti-inflammatory drugs, antifungal medications, and many antibiotics (1 point)
5. T=tobacco use in two years (2 points)
6. R=non-white race (2 points).

It helps to choose anticoagulants to prevent thromboembolism in patients with atrial fibrillation. If the SAMe-TT_2R_2 score is greater than 2 point, it showed risk at INR level, not high maintenance level[15]. Therefore, this scoring system is recommended[16-19].

The present study was to examine the SAMe-TT_2R_2 score in Thai patients comparing to the forecast of INR levels after taking Warfarin.

Materials and Methods

The present study was conducted retrospectively at Pranangklao Hospital, between January 1, 2019 and October 31, 2020. All patients 18 years or older diagnosed as having atrial fibrillation and been taking Warfarin for more than a year were enrolled. The following patients were excluded 1) patients who stop taking Warfarin during the treatment program for four months or less, 2) patients with a history of metallic heart valve replacement surgery, and 3) patients who were hospitalized during the medical program for four months or less.

Sample size estimation was calculated based on the infinite population mean calculation technique. Using the previous data by Reid et al, the standard deviation and the error approximated at 17 and 3 (ref.), with type I & II error set at 0.05 and 0.2, respectively, the size was 124.

The labile INR were defined as TTR (by Rosendalls linear interpolation method) of patients having less than 65 percent of the follow-up period. It showed that the occurrence of the ischemic stroke appeared when INR was less than 2, and the bleeding event appeared when INR is more than 3.

The present study protocol was approved by the Institutional Review Board, No. EC19/2563. The present study complied with the Declaration of Helsinki, CIOMS Guidelines and International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Statistical analysis

Descriptive statistics, including frequency and percentage, were used for categorical variables. Continuous variables were reported as mean and standard deviation (SD). The distribution of variables was examined by the Kolmogorov-Smirnov test. The comparison of normally distributed continuous variables between two groups was used the unpaired student t-test and chi-square test was used for categorical data, a p-value of less than 0.05 was considered to be statistically significant. The diagnostic test was evaluated by using sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs). IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses.

Results

According to the Pranangklao Hospital database, 130 patients were diagnosed with atrial fibrillation and prescribed warfarin between January 1, 2019 and October 31, 2020.

Baseline characteristics are shown in Table 1. The average age was 67.5±10.2 years, and 63 (48.5%) of the patients were male. An average INR test per patient was 6±3 tests. The average SAMe-TT_2R_2 score was 3.2±0.8. The average CHA_2DS_2-VASc score was 3.3±1.4.

Patients had hypertension 88.5%, diabetes mellitus 32.3%, chronic kidney disease 32.3%, coronary artery disease 10.8%, and previous stroke or transient ischemic attack (TIA) 26.5%. Most patients had hypertension and dyslipidemia. Most patients were prescribed beta-blockers. Most patients had TTR of less than 65%

The proportions of Thai atrial fibrillation patients with labile INR between SAMe-TT_2R_2 Score of 2 and SAMe-TT_2R_2 Score more than 3 are shown in Figure 1. The present study showed the proportion of atrial fibrillation patients with labile INR were also found in patient with SAMe-TT_2R_2 score more than or equal to 3. This finding was statistically significant ($p<0.001$).

The SAMe-TT_2R_2 score and SAMe-TT_2R_2 score excluding race could be used for prediction of labile INR as shown in Table 2. The present study showed the sensitivity, specificity, PPV, and NPV of edge cut-off SAMe-TT_2R_2 score could predict labile INR the same as SAMe-TT_2R_2 score excluding race.

When the cut-off score is increased, the sensitivity decreased, and the specificity increased. The PPV was in the range of 73.3 to 75.0% in SAMe-TT_2R_2 score

Table 1. Baseline characteristics of the patients

Demographic data	Total (n=130); n (%)
Age (years); mean±SD	67.5±10.2
Sex: male	63 (48.5)
Weight (kg); mean±SD	68±16.5
Height (cm); mean±SD	162.3±7.9
Body mass index (kg/m^2); mean±SD	25.7±5.5
Smoking status	4 (2.7)
SAMe-TT_2R_2 score; mean±SD	3.2±0.8
CHA_2DS_2-VASc score; mean±SD	3.3±1.4
Medical history	
Hypertension	115 (88.5)
Diabetes mellitus	42 (32.3)
CKD (GFR <60 mL/minute)	42 (32.3)
Dyslipidemia	104 (80.0)
Hepatic disease	2 (1.5)
Coronary artery disease	14 (10.8)
Previous stroke/TIA	34 (26.2)
Medication	
Beta-blocker	105 (80.8)
Non-dihydropyridine CCB	6 (4.6)
Digoxin	12 (9.2)
Nitrate	8 (6.2)
ASA	24 (18.5)
Clopidogrel	7 (5.4)
TTR (%)	
<65	86 (66.2)
>65	44 (33.8)

CKD=chronic kidney disease; GFR=glomerular filtration rate; TIA=transient ischemic attack; CCB=calcium channel blocker; ASA=aspirin; TTR=time in therapeutic range

and 73.3 to 75.0 in SAMe-TT_2R_2 score excluding race.

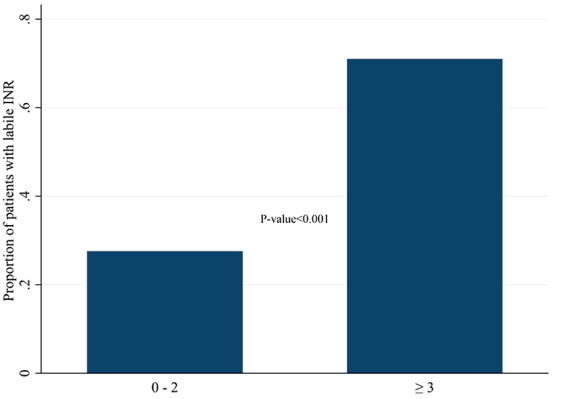

Figure 1. The proportion of Thai AF patients with labile INR between SAMe-TT_2R_2 score of 2 or less and SAMe-TT_2R_2 score of 3 or more.

In addition, the area under curve (AUC) decreased when the cut-off score increased. The comparison of AUC of SAMe-TT_2R_2 with or without race was found to be the same.

Discussion

The present study showed that SAMe-TT_2R_2 score was significantly associated with labile INR, while high TTR was associated with a good outcome. The previous study showed that assessment of TTR control in atrial fibrillation patients with TTR greater than 65% who received warfarin for anticoagulants had less mortality[20].

The GARFIELD-AF registry[20] showed that the level of anticoagulation controls in Asians was lower than those in Western population.

CYP2C9 and VKORC1 polymorphism in Asian atrial fibrillation patients could affect labile INR. That explained the reason the Asian patients had more bleeding than Western atrial fibrillation patients.

Table 2. The SAMe-TT_2R_2 score for the prediction of labile INR

Cut-off score	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	AUC (%) (95% CI)
SAMe-TT_2R_2 score					
>3	89.5 (81.1 to 95.1)	36.4 (22.4 to 52.2)	73.3 (63.8 to 81.5)	64.0 (42.5 to 82.0)	62.9 (55.1 to 70.8)
>4	43.0 (32.4 to 54.2)	70.5 (54.8 to 83.2)	74.0 (59.7 to 85.4)	38.8 (28.1 to 50.3)	56.7 (48.1 to 65.4)
>5	7.0 (2.6 to 14.6)	95.5 (84.5 to 99.4)	75.0 (34.9 to 96.8)	34.4 (26.1 to 43.6)	51.2 (47.1 to 55.3)
SAMe-TT_2R_2 score exclude race					
>1	89.5 (81.1 to 95.1)	36.4 (22.4 to 52.2)	73.3 (63.8 to 81.5)	64.0 (42.5 to 82.0)	62.9 (55.1 to 70.8)
>2	43.0 (32.4 to 54.2)	70.5 (54.8 to 83.2)	74.0 (59.7 to 85.4)	38.8 (28.1 to 50.3)	56.7 (48.1 to 65.4)
>3	7.0 (2.6 to 14.6)	95.5 (84.5 to 99.4)	75.0 (34.9 to 96.8)	34.4 (26.1 to 43.6)	51.2 (47.1 to 55.3)

PPV=positive predictive value; NPV=negative predictive value; AUC=area under curve

The p-value for compare performance between SAMe-TT_2R_2 score with or without race is 1.000

Previous studies in Thailand showed increasing proportion of atrial fibrillation patients with labile INR was also found increase in SAMe-TT_2R_2 score[21,22]. The atrial fibrillation patients with SAMe-TT_2R_2 score of 3 or more had no significant difference in proportion of labile INR from patients with SAMe-TT_2R_2 score of 2 or less, with borderline significance ($p=0.056$)[21].

In addition, another study in Thailand showed the sensitivity decreased and the specificity increased, when the SAMe-TT_2R_2 cut-offs score increased[23].

According to the present study, it showed the SAMe-TT_2R_2 score excluding race and the SAMe-TT_2R_2 score with race could be used to predict the labile INR control in Thai patients with atrial fibrillation receiving warfarin. If The SAMe-TT_2R_2 score excluding race was high, the specificity of labile INR control in Thai patients was accordingly high with low sensitivity. The comparison of AUC of SAMe-TT_2R_2 score with or without race was found to be no different.

However, the present study had some limitations. First, the study population was recruited from a single center. The study might be generalizable. Second, the present study was a retrospective study with a small sample size. The study might have been underpowered. In conclusion, the present study was done in a small number of Thai patients. Therefore, it should be done in a larger study in the future

Conclusion

The SAMe-TT_2R_2 score is a universal score to predict labile INR. Atrial fibrillation in Thai patients is useful for prediction.

What is already known on this topic?

The SAMe-TT_2R_2 score could predict the labile INR in Thai patients with atrial fibrillation receiving warfarin.

What this study adds?

Excluding Caucasian atrial fibrillation patients, the SAMe-TT_2R_2 score is useful to predict the labile INR in atrial fibrillation in Thai patients receiving warfarin.

Conflicts of interest

The author declares that they have no conflicts of interest.

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