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Use of simplified HAS-BLED score in patients with atrial fibrillation receiving warfarin

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Abstract

Background: Oral anticoagulant drugs are proven to prevent thromboembolism in patients with atrial fibrillation (AF). To date, HAS-BLED score is used to assess bleeding risk. This study was conducted to compare simplified HAS-BLED (sHAS-BLED) with conventional HAS-BLED (cHAS-BLED) scores.

Methods: This retrospective study recruited patients with AF receiving warfarin among July 2013 to December 2018 in Central Chest Institute of Thailand. The cHAS-BLED score used the time in therapeutic range less than 70% as labile INR, whereas sHAS-BLED score used SAMe-TT_2R_2 score of 3 or more as a substitute for labile INR. A paired Student's *t* test was used to compare sHAS-BLED and cHAS-BLED. The Pearson's correlation was used to assess the correlation of sHAS-BLED to cHAS-BLED scores. The Bland-Altman plot was used to confirm the agreement of individual sHAS-BLED to cHAS-BLED score.

Results: A total of 126 AF patients were enrolled. The average age, SAMe-TT_2R_2 score, and cHAS-BLED score were 70.52 ± 10.37 years, 3.53 ± 1.03, and 2.03 ± 0.95, respectively. The sHAS-BLED score was not statistically significantly different compared with cHAS-BLED score ($P = .08$). The sHAS-BLED and cHAS-BLED scores had a very strong correlation with a correlation coefficient of .86 ($P < .01$). The Bland-Altman plot was performed to confirm the agreement of individual sHAS-BLED to cHAS-BLED scores.

Conclusions: The sHAS-BLED was not statistically significantly different compared with cHAS-BLED and can be used in clinical practice. However, larger clinical trial will be needed to prove whether sHAS-BLED can predict bleeding risk in the future.

KEYWORDS

labile INR, poor anticoagulation control, SAMe-TT_2R_2, simplified HAS-BLED, time in therapeutic range

1 | INTRODUCTION

Atrial fibrillation (AF) is a common cardiac arrhythmia in clinical practice. Stroke prevention is paramount importance in AF management. To date, only oral anticoagulant drugs (OACs) are proven to prevent thromboembolism in those patients.[1] According to standard clinical practice guidelines recommend OACs should be prescribed in AF patients with non-sex CHA_2DS_2-VASc of 1 or more (score of ≥ 1 in a male or ≥2 in a female).[2–4]

Vitamin-K antigonists (VKAs) especially warfarin are the most common oral anticoagulant drugs prescribed in those patients. International normalized ratio (INR) is a laboratory test for assessing anticoagulation control.[5] Quality of anticoagulation control is measured by time in therapeutic range (TTR) using Rosendaal method.[6] Previous clinical trials have demonstrated that poor TTR is associated with adverse events including thromboembolism, bleeding, and/or mortality.[7,8]

Apostolakis et al proposed using SAMe-TT_2R_2 (Gender female, Age <60 years, Medical history [more than two comorbidities], Treatment [interacting drugs, eg, amiodarone for rhythm control], Tobacco use [doubled], Race [doubled]) score to predict poor TTR.[9] Several clinical trials have demonstrated the score of 3 or more could predict poor anticoagulation control.[10–14]

Until now, standard clinical practice guidelines recommend the use of HAS-BLED score to predict bleeding risk in those patients.[2–4] Labile INR in those score is defined as poor TTR (eg, TTR less than 60%).[15] However, TTR is a cumbersome calculated problem in clinical practice. This study was conducted to simplify HAS-BLED score by using SAMe-TT_2R_2 score of 3 or more as a substitute for labile INR and compared simplified HAS-BLED (sHAS-BLED) with conventional HAS-BLED (cHAS-BLED) scores.

2 | METHODS

The present study was the retrospective observational study. AF patients receiving warfarin were recruited among July 2013 to December 2018 in Central Chest Institute of Thailand. The patients with age less than 18 years, duration of warfarin usage less than 1 year, each INR during follow-up visit lasting more than 6 months, hospitalization during study, warfarin interruption from surgery, intervention or any causes were excluded. The study protocol was approved by the Institutional Review Board. The present study complied with the Declaration of Helsinki.

HAS-BLED score is defined following 2010 ESC guidelines for the management of AF.[16] Because of target INR should be ≥70% ideally[3], labile INR is defined as TTR less than 70% in HAS-BLED score in this study. TTR is calculated by using Rosendaal method.[6]

Conventional HAS-BLED (cHAS-BLED) score used the TTR less than 70% as labile INR, while simplified HAS-BLED (sHAS-BLED) score used SAMe-TT_2R_2 score of 3 or more as a substitute for labile INR.

The author determined 0.05 for type I error and 0.20 for type II error with 80% power. The estimated standard deviation of difference between sHAS-BLED and cHAS-BLED was 2 points. The nonsignificant difference of mean between sHAS-BLED and cHAS-BLED was determined as 0.5 point. A sample size of 126 patients or more was calculated by the *t* test for dependent means. A paired Student's *t* test was used to compare sHAS-BLED and cHAS-BLED scores if data distribution was normal. Wilcoxon signed-rank test was used if data distribution was skewed. The Pearson's correlation was used to assess correlation of sHAS-BLED to cHAS-BLED scores. The Bland-Altman plot was used to confirm the agreement of individual sHAS-BLED to cHAS-BLED scores. The demographic and clinical data were interpreted by using descriptive statistics. The categorical data are presented as frequency and percentage. The continuous variables are presented as mean ± standard deviation if data distribution is normal and median ± interquartile range if data

TABLE 1 Baseline characteristics of the patients

Demographic data	Total n = 126 n (%) or mean ± SD
Age (y)	70.52 ± 10.37
Male gender	53.20
Paroxysmal AF	28.60
LVEF (%)	57.62 ± 16.92
SAMe-TT_2R_2 score	3.53 ± 1.03
cHAS-BLED score	2.03 ± 0.95
Time in therapeutic range (%)	51.40 ± 24.93
eGFR (ml/min/1.73 m^2)	66.75 ± 21.01
Medical history	
Diabetes mellitus	28.57
Hypertension	74.60
Hypercholesterolemia	78.60
Coronary artery disease	24.60
Peripheral artery disease	0
Chronic kidney disease	3.90
Previous stroke/TIA	19.05
History of heart failure	35.70
Liver disease	0.80
Pulmonary disease	0.80
Medications	
Beta-blockers	73.02
Nondihydropyridine CCBs	7.10
Digoxin	20.60
Antiplatelets	10.32
Warfarin	100.00
Amiodarone	5.56
Flecainide	2.40

Abbreviations: AF, atrial fibrillation; CCBs, calcium channel blockers; cHAS-BLED, conventional HAS-BLED; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; min, minute; ml, millimeter; n, numbers; SD, standard deviation; TIA, transient ischemic attack.

distribution is skewed. A *P*-value of .05 or less was considered the statistical significance.

3 | RESULTS

A total of 126 AF patients were enrolled. The average age was 70.52 ± 10.37 years. A half of those were male gender. About one-third of those were paroxysmal AF. The average SAMe-TT_2R_2 score was 3.53 ± 1.03. The average cHAS-BLED score was 2.03 ± 0.95. Of 104 patients with SAMe-TT_2R_2 score of 3 or more, 20 patients (19.23%) had TTR ≥ 70%. Most patients had hypertension and hypercholesterolemia. About one-fifth of those experienced stroke and/or transient ischemic attack (TIA). Only 5.56% of those used concomitant amiodarone. Baseline characteristics are shown in Table 1. The distribution of patients in SAMe-TT_2R_2 score was shown in Figure 1.

The sHAS-BLED score was compared with cHAS-BLED score by using paired Student's *t* test. This study demonstrated no statistically significant difference between sHAS-BLED and cHAS-BLED scores (*P* = .08) (Table 2).

The sHAS-BLED score was analyzed by using Pearson's correlation relative to cHAS-BLED score. The sHAS-BLED and cHAS-BLED scores had a very strong correlation with a correlation coefficient of .86 (*P* < .01) (Figure 2).

The Bland-Altman plot was performed to confirm the agreement of individual sHAS-BLED to cHAS-BLED scores (Figure 3).

Patients with sHAS-BLED score of 3 or more had a history of bleeding for 68.75% compared with 67.39% in those with cHAS-BLED score of 3 or more.

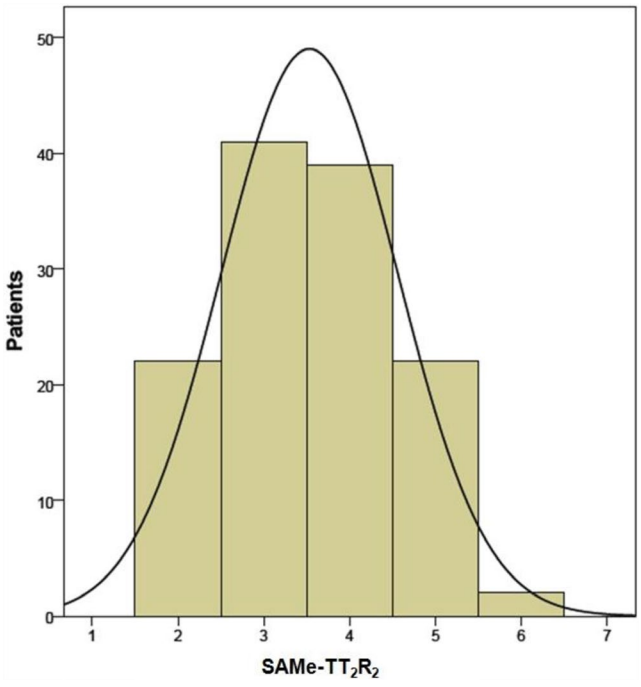

FIGURE 1 The distribution of patients in SAMe-TT_2R_2 score

TABLE 2 Comparison between sHAS-BLED and cHAS-BLED score

	sHAS-BLED score	cHAS-BLED score	*P*-value
Mean ± SD	2.27 ± 0.92	2.19 ± 0.97	.08

Abbreviations: cHAS-BLED, conventional HAS-BLED; SD, standard deviation; sHAS-BLED, simplified HAS-BLED.

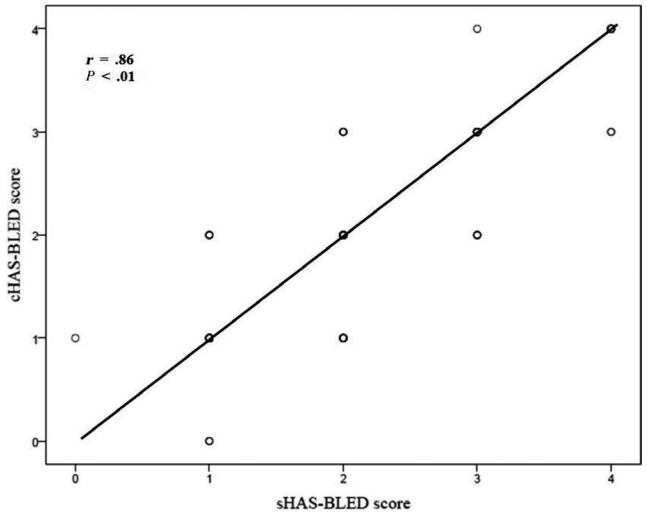

FIGURE 2 Relationship between sHAS-BLED and cHAS-BLED scores

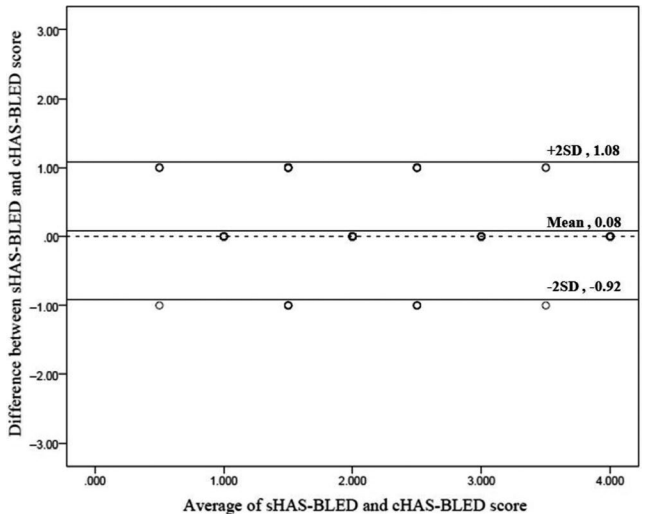

FIGURE 3 Bland-Altman plot confirmed the agreement of individual sHAS-BLED to cHAS-BLED scores

4 | DISCUSSION

To the best of our knowledge, this trial was the first study that has demonstrated sHAS-BLED score could be used in AF patients receiving warfarin. The sHAS-BLED and cHAS-BLED scores were comparable and they had a very strong correlation.[17] There was also

the agreement of individual sHAS-BLED and cHAS-BLED scores by using the Bland-Altman plot.

Previous trials showed the cHAS-BLED score could be used to predict bleeding events in AF patients.[15] Labile INR in cHAS-BLED was defined as TTR < 60% in those trials including several standard clinical practice guidelines.[16,18] Previous clinical trials have demonstrated that poor TTR is associated with adverse events including thromboembolism, bleeding, and/or mortality.[7,8] To date, well-controlled VKAs has been used TTR more than 70% as reflect in recommendations of recent clinical practice guidelines.[2,3,18]

This trial defined the labile INR by using TTR < 70% as a substitute for those < 60% in cHAS-BLED score because of SAMe-TT_2R_2 score was proved to predict labile INR < 65%-70% in previous trials.[9–13] Nevertheless, labile INR in cHAS-BLED score in this trial may be different from those in previous HAS-BLED score trials.

The sHAS-BLED score could be used to improve the easier HAS-BLED score calculation by using SAMe-TT_2R_2 as substitute for labile INR without TTR calculating by using Rosendaal method. Additionally, the labile INR in cHAS-BLED cannot be counted in AF patients initiating on warfarin because of no previous INR data. The SAMe-TT_2R_2 score can be used to predict labile INR in those patients and calculate sHAS-BLED by using SAMe-TT_2R_2 score of 3 or more as a substitute for labile INR.

However, these trials had some limitations. First, definition of labile INR in this trial was different from previous clinical trials as mentioned before. Previous clinical trials proved that HAS-BLED score for prediction of bleeding events by using TTR < 60% as labile INR, but this trial used TTR < 70% as labile INR in cHAS-BLED score. However, recent clinical practice guidelines recommend TTR ≥ 70% should be used in most AF patients receiving warfarin. Second, this trial had a small AF patients compared with previous trials and there were only Asian patients, so it was a limitation in other racial population such as Caucasian. Third, sHAS-BLED score was not still proved for assessment of bleeding risk prediction. Nevertheless, patients with sHAS-BLED score of 3 or more had a history of bleeding comparable to those with cHAS-BLED score of 3 or more. However, larger clinical trial will be needed to prove whether sHAS-BLED can predict bleeding risk in the future. Finally, this study was a retrospective study and there may be some missing data. However, this trial was the first study that has demonstrated sHAS-BLED score was more simplified and comfortable to use in clinical practice.

5 | CONCLUSIONS

The sHAS-BLED by using SAMe-TT_2R_2 score of 3 or more as a substitute for labile INR was not statistically significantly different compared with cHAS-BLED score and can be used in clinical practice. However, larger clinical trial will be needed to prove whether sHAS-BLED can predict bleeding risk in the future.

CONFLICT OF INTEREST

Authors declare no conflict of interest for this article.

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