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

Komsing Methavigul MD, FRCPT | Ratikorn Methavigul MD, FRCPT

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-TT₂R₂ 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-TT₂R₂ 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-TT₂R₂, simplified HAS-BLED, time in therapeutic range
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. According to standard clinical practice guidelines recommend OACs should be prescribed in AF patients with non-sex CHA2DS2-VASc of 1 or more (score of ≥ 1 in a male or ≥ 2 in a female). Vitamin-K antagonists (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. Quality of anticoagulation control is measured by time in therapeutic range (TTR) using Rosendaal method. Previous clinical trials have demonstrated that poor TTR is associated with adverse events including thromboembolism, bleeding, and/or mortality. Apostolakis et al proposed using SAMe-TT2R2 (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. Several clinical trials have demonstrated the score of 3 or more could predict poor anticoagulation control.

Until now, standard clinical practice guidelines recommend the use of HAS-BLED score to predict bleeding risk in those patients. Labile INR in those score is defined as poor TTR (eg, TTR less than 60%). However, TTR is a cumbersome calculated problem in clinical practice. This study was conducted to simplify HAS-BLED score by using SAMe-TT2R2 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. Because of target INR should be ≥70% ideally, labile INR is defined as TTR less than 70% in HAS-BLED score in this study. TTR is calculated by using Rosendaal method.

Conventional HAS-BLED (cHAS-BLED) score used the TTR less than 70% as labile INR, while simplified HAS-BLED (sHAS-BLED) score used SAMe-TT2R2 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 |
|------------------|--------------|
| Age (y)          | 70.52 ± 10.37|
| Male gender      | 53.20        |
| Paroxysmal AF    | 28.60        |
| LVEF (%)         | 57.62 ± 16.92|
| SAMe-TT2R2 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 m²)| 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$_2$R$_2$ score was 3.53 ± 1.03. The average cHAS-BLED score was 2.03 ± 0.95. Of 104 patients with SAMe-TT$_2$R$_2$ 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$_2$R$_2$ 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.

| 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.

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. 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.\textsuperscript{15} Labile INR in cHAS-BLED was defined as TTR < 60% in those trials including several standard clinical practice guidelines.\textsuperscript{16,18} Previous clinical trials have demonstrated that poor TTR is associated with adverse events including thromboembolism, bleeding, and/or mortality.\textsuperscript{7,8} To date, well-controlled VKAs has been used TTR more than 70% as reflect in recommendations of recent clinical practice guidelines.\textsuperscript{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-\textsuperscript{2T,2R} score was proved to predict labile INR < 65%-70% in previous trials.\textsuperscript{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-\textsuperscript{2T,2R} 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-\textsuperscript{2T,2R} score can be used to predict labile INR in those patients and calculate sHAS-BLED by using SAME-\textsuperscript{2T,2R} 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-\textsuperscript{2T,2R} 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.

ORCID

Komsing Methavigul https://orcid.org/0000-0002-8739-203X

REFERENCES

1. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Arch Intern Med. 1994;154:1449–57.
2. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation. Eur Heart J. 2016;37(38):2893–962.
3. Lip G, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B, et al. Antithrombotic therapy for atrial fibrillation. Chest. 2018;154(5):1121–201.
4. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. J Am Coll Cardiol. 2019;74(1):104–32.
5. Hirsh J, Fuster V, Ansell J, Halperin JL. American Heart Association/ American College of Cardiology Foundation guide to warfarin therapy. J Am Coll Cardiol. 2003;41(9):1633–52.
6. Rosendaal FR, Cannegieter SC, van der Meer JF, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost. 1993;69(3):236–9.
7. Wan YI, Heneghan C, Perera R, Roberts N, Hollowell J, Glasziou P, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. Circ Cardiovasc Qual Outcomes. 2008;1(2):84–91.
8. Haas S, ten Cate H, Accetta G, Anghiaiukisri P, Bassand J-P, Camm AJ, et al. Quality of vitamin K antagonist control and 1-year outcomes in patients with atrial fibrillation: a global perspective from the GARFIELD-AF Registry. PLoS ONE. 2016;11(10):e0164076.
9. Apostolakis S, Sullivan RM, Olshansky B, Lip G. Factors affecting quality of anticoagulation control among patients with atrial fibrillation on warfarin: the SAME-\textsuperscript{2T,2R} score. Chest. 2013;144(5):1555–63.
10. Lip G, Hagenoer K, Saint-Etienne C, Fauchier L. Relationship of the SAME-\textsuperscript{2T,2R} score to poor-quality anticoagulation, stroke, clinically relevant bleeding, and mortality in patients with atrial fibrillation. Chest. 2014;146(3):719–26.
11. Proietti M, Lane DA, Lip G. Relation of the SAME-\textsuperscript{2T,2R} score to quality of anticoagulation control and thromboembolic events in atrial fibrillation patients: observations from the SPORTIF trials. Int J Cardiol. 2016;216:668–72.
12. Chan PH, Hai JJ, Chee EW, Li WH, Tse HF, Wong I, et al. Use of the SAME-\textsuperscript{2T,2R} score to predict good anticoagulation control with warfarin in Chinese patients with atrial fibrillation: relationship to ischemic stroke incidence. PLoS ONE. 2016;11(3):e0150674.
13. Bernaïtis N, Ching CK, Chen L, Hon JS, Teo SC, Davey AK, et al. The sex, age, medical history, treatment, tobacco use, race risk (SAME \textsuperscript{2T,R2} score predicts warfarin control in a Singaporean population. J Stroke Cerebrovasc Dis. 2017;26(1):64–9.
14. Methavigul K. Proportion of Thai patients with atrial fibrillation receiving warfarin with labile INR in each group of SAME-\textsuperscript{2T,2R} score. J Med Assoc Thai. 2018;101(2):189–93.
15. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip G. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010;138(5):1093–100.
16. Camm AJ, Kirchhof P, Lip G, et al. Guidelines for the management of atrial fibrillation. Eur Heart J. 2010;31(19):2369–429.
17. Chan YH. Biostatistics 104: correlational analysis. Singapore Med J. 2003;44(12):614–9.
18. Chiang C-E, Okumura K, Zhang S, Chao T-F, Siu C-W, Wei Lim T, et al. 2017 consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. J Arrhythm. 2017;33(4):345–67.

How to cite this article: Methavigul K, Methavigul R. Use of simplified HAS-BLED score in patients with atrial fibrillation receiving warfarin. J Arrhythmia. 2019;35:711–715. https://doi.org/10.1002/joa3.12225