*Original Article*

# Use of Simplified HAS-BLED Score for Predicting Bleeding Events in Anticoagulated Patients with Atrial Fibrillation

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***Objective***: To demonstrate bleeding risk prediction of simplified HAS-BLED (sHAS-BLED) score in anticoagulated patients with atrial fibrillation (AF).

***Materials and Methods***: AF patients receiving warfarin were retrospectively recruited in Central Chest Institute of Thailand between October 2012 and December 2017. The main outcome was total bleeding including major bleeding, clinically relevant non-major bleeding or minor bleeding. The chi-square test or Fisher's exact test was used to compare the main outcome between sHAS-BLED and conventional HAS-BLED (cHAS-BLED) scores. A sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of sHAS-BLED were calculated. The discrimination performances of sHAS-BLED and cHAS-BLED scores were demonstrated with c-statistics.

***Results***: One hundred ten patients were recruited. The mean age was 70.53±9.58 years. The average sHAS-BLED and cHAS-BLED scores were 2.23±0.79 and 1.95±0.83, respectively. The patients with sHAS-BLED score of 3 or more had 15 total bleeding events (37.50%) while those with score of less than 3 had 13 total bleeding events (18.57%). Those with sHAS-BLED score of 3 or more had more total bleeding than those with score of less than 3 with statistical significance (odds ratio 2.63; 95% CI 1.09 to 6.25; p=0.049). A sensitivity, specificity, PPV, and NPV of sHAS-BLED score were 53.57%, 69.51%, 37.50%, and 81.43%, respectively. The discrimination performances of sHAS-BLED and cHAS-BLED scores were demonstrated with c-statistics of 0.65 and 0.67, respectively.

***Conclusion***: The sHAS-BLED score can be used for bleeding risk prediction in anticoagulated AF patients compared with cHAS-BLED score.

***Keywords***: Simplified HAS-BLED, Atrial fibrillation, Anticoagulant, Bleeding, SAMe-$TT_2R_2$

Received 2 November 2020 | Revised 15 February 2021 | Accepted 15 February 2021

**J Med Assoc Thai 2021;104(5):802-6**

**Website:** http://www.jmatonline.com

Stroke prevention is of paramount importance in patients with atrial fibrillation (AF). Oral anticoagulants (OACs) are prescribed for prevention of ischemic stroke in these patients[1]. To date, recent international guidelines suggest the use of OACs in those with $CHA_2DS_2$-VASc score of 1 or more in male patients and of 2 or more in female patients[2-4]. However, several AF patients with OACs suffered from bleeding events such as intracranial hemorrhage, gastrointestinal bleeding. HAS-BLED score is the suggested risk scoring system for predicting bleeding risk in AF patients[2-5].

HAS-BLED score has been recommended to use for bleeding risk prediction in AF patients in the previous European guideline since 2010[6]. This risk scoring system has a limitation because the definition of labile international normalized ratio (INR) is poor time in therapeutic range (TTR) of less than 60%, which is difficult to calculate in clinical practice. Recently, Methavigul et al proposed a simplified HAS-BLED (sHAS-BLED) score including SAMe-$TT_2R_2$ score[7-13] incorporated into conventional HAS-BLED (cHAS-BLED) score[14]. Labile INR in sHAS-BLED score was defined as SAMe-$TT_2R_2$ score of 3 or more. The present study demonstrated that sHAS-BLED and cHAS-BLED score had comparable correlation and agreement[14].

Currently, there is no data about risk prediction of bleeding events of sHAS-BLED score in AF patients receiving warfarin. The present study was conducted to demonstrate bleeding risk prediction of those risk score.

## Materials and Methods

AF patients receiving warfarin aged 18 years or more were retrospectively recruited in Central Chest Institute of Thailand between October 2012 and December 2017. The patients with contraindication

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**How to cite this article:**

Methavigul K. Use of Simplified HAS-BLED Score for Predicting Bleeding Events in Anticoagulated Patients with Atrial Fibrillation. J Med Assoc Thai 2021;104:802-6.

doi.org/10.35755/jmedassocthai.2021.05.12142

of warfarin or duration of warfarin use below one year, INR measurement during follow-up visit of more than six months apart, hospital admission during the study, any causes of warfarin discontinuation, patients with prosthetic heart valve or mitral valve repair, thrombocytopenia with a platelet count below 100,000/mm$^3$, myeloproliferative disorders, hyperviscosity syndrome, pregnancy, or patients participating in other concealed study were excluded. The present study protocol was approved by the Human Research Ethics Committee of Central Chest Institute of Thailand (No.041/2563). The present study was compliant with the Declaration of Helsinki and was registered on Thai Clinical Trials Registry (TCTR20200105005).

The definitions of cHAS-BLED and sHAS-BLED scores were following the European standard clinical practice guideline[6] and Methavigul et al[14], respectively. The main outcome was total bleeding including major bleeding, clinically relevant non-major bleeding (CRNMB) or minor bleeding. Major bleeding was defined according to the International Society on Thrombosis and Haemostasis (ISTH)[15]. The definition of CRNMB was non-major bleeding requiring medical attention. Bleeding other than major or CRNMB was minor.

The present study required 0.05 for type I error and 0.10 for type II error with 90% power. The author expected 1% and 23% for bleeding events in patients with sHAS-BLED score of less than 3 and those with score of 3 or more, respectively[14]. Therefore, the ratio of estimated bleeding events in those with sHAS-BLED score of 3 or more to those with score less than 3 was 2. At least 108 patients were calculated to compare the two populations by chi-square test.

The demographic data were analyzed by using descriptive statistics. The categorical data were presented as frequency and percentage. The continuous data were presented as mean ± standard deviation. The chi-square test or Fisher's exact test was used to compare the main outcome between sHAS-BLED and cHAS-BLED scores. A sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of sHAS-BLED were calculated. The discrimination performances of sHAS-BLED and cHAS-BLED scores were demonstrated with c-statistics. A p-value of 0.05 or less was statistically significant.

## Results

One hundred ten patients were recruited. The mean age was 70.53±9.58 years. More than half of these were male (55.50%). There was paroxysmal AF in about one-third of the patients. The average sHAS-BLED and cHAS-BLED scores were 2.23±0.79 and 1.95±0.83, respectively. The average TTR was 52.78±24.01%. Almost all of patients had hypertension (80.90%) and hypercholesterolemia (80.90%). Those were prescribed concomitant antiplatelets in 20% of patients. The distribution of patients according to sHAS-BLED score is shown in Figure 1. The baseline characteristics are shown in Table 1.

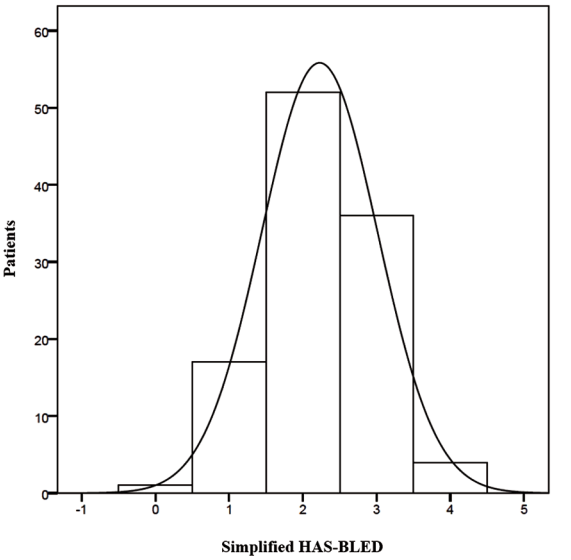


**Figure 1.** The distribution of patients according to sHAS-BLED score.

Patients with sHAS-BLED score of 3 or more had 15 total bleeding events (37.50%) including two major bleeding or CRNMB events and 13 minor bleeding events, while those with score of less than 3 had 13 total bleeding events (18.57%) including one major bleeding or CRNMB events and 12 minor bleeding events. Those with sHAS-BLED score of 3 or more had more total bleeding than those with score of less than 3 with statistical significance (odds ratio 2.63; 95% CI 1.09 to 6.25; p=0.049). Although there was more major bleeding or CRNMB events and more minor bleeding events in those with score of 3 or more, there was also no statistical significance compared with those with score of less than 3. However, patients with sHAS-BLED score of 3 or more had a trend in more major bleeding or CRNMB and minor bleeding. Comparison of total bleeding, major bleeding or CRNMB and minor bleeding between AF patients with sHAS-BLED score of 3 or more and those with score of less than 3 is shown in Table 2.

A sensitivity, specificity, PPV, and NPV of sHAS-

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

| Demographic data | Total (n=110); n (%) |
|---|---|
| Age (years); mean±SD | 70.53±9.58 |
| Sex: male | 61 (55.45) |
| Paroxysmal AF | 30 (27.27) |
| SAMe-$TT_2R_2$ score; mean±SD | 3.24±0.85 |
| Simplified HAS-BLED score; mean±SD | 2.23±0.79 |
| Conventional HAS-BLED score; mean±SD | 1.95±0.83 |
| Time in therapeutic range (%); mean±SD | 52.78±24.01 |
| Medical history | |
| Diabetes mellitus | 31 (28.18) |
| Hypertension | 89 (80.91) |
| Hypercholesterolemia | 89 (80.91) |
| Coronary artery disease | 33 (30.00) |
| Peripheral artery disease | 1 (0.91) |
| Chronic kidney disease | 43 (39.09) |
| Previous stroke/TIA | 20 (18.18) |
| History of heart failure | 38 (34.55) |
| Liver disease | 0 (0.00) |
| Pulmonary disease | 5 (4.55) |
| LVEF (%); mean±SD | 55.21±19.01 |
| Serum creatinine (mg/dL); mean±SD | 1.02±0.28 |
| eGFR (mL/minute/1.73 $m^2$); mean±SD | 68.02±19.06 |
| Medications | |
| Beta-blockers | 84 (76.36) |
| Nondihydropyridine CCBs | 7 (6.36) |
| Digoxin | 28 (25.45) |
| Antiplatelets | 22 (20.00) |
| Warfarin | 110 (100) |
| Amiodarone | 10 (9.09) |
| Flecainide | 1 (0.91) |

SD=standard deviation; AF=atrial fibrillation; TIA=transient ischemic attack; LVEF=left ventricular ejection fraction; mg/dL=milligrams per deciliter; eGFR=estimated glomerular filtration rate; mL=millimeter; CCBs=calcium channel blockers

BLED score were 53.57%, 69.51%, 37.50%, and 81.43%, respectively (Table 3). The discrimination performances of sHAS-BLED and cHAS-BLED scores were demonstrated with c-statistics of 0.65 and 0.67, respectively. The receiver operating characteristic (ROC) curves of sHAS-BLED and cHAS-BLED scores are shown in Figure 2.

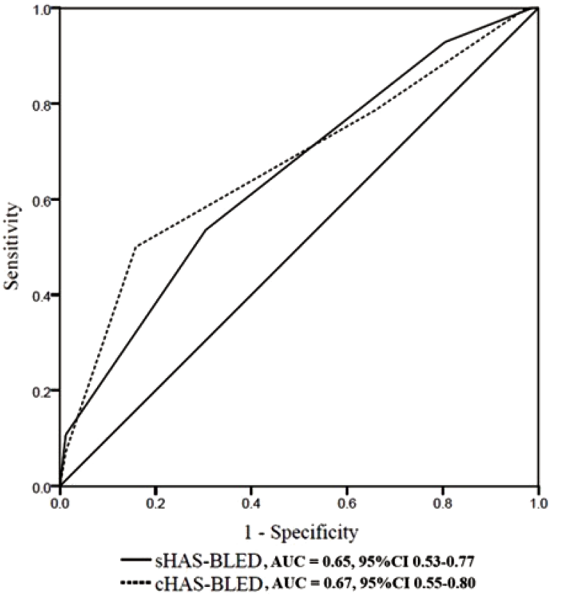


**Figure 2.** Comparison of ROC curve between sHAS-BLED and cHAS-BLED scores.

## Discussion

Based on current knowledge, HAS-BLED score is suggested for the bleeding risk assessment in AF patients receiving OACs. However, this risk score has a problem about cumbersome calculation of TTR in clinical practice because the definition of labile INR depends on TTR. This trial revealed that sHAS-BLED score could be used for prediction of bleeding risk in AF patients receiving warfarin. Previous trial has shown that sHAS-BLED and cHAS-BLED scores had comparable correlation and agreement[14]. However, that trial had some limitations. First, that trial used a different definition of labile INR compared with cHAS-BLED score. That trial determined the labile

**Table 2.** Comparison of total bleeding, major bleeding or CRNMB and minor bleeding between AF patients with sHAS-BLED score ≥3 and those with score <3

| Bleeding events | sHAS-BLED ≥3 (n=40); n (%) | sHAS-BLED <3 (n=70); n (%) | OR (95% CI) | p-value |
|---|---|---|---|---|
| Total bleeding | 15 (37.50) | 13 (18.57) | 2.63 (1.09 to 6.25) | 0.049 |
| Major bleeding or CRNMB | 2 (5.00) | 1 (1.43) | 3.57 (0.32 to 50) | 0.619 |
| Minor bleeding | 13 (32.50) | 12 (17.14) | 2.33 (0.93 to 5.88) | 0.107 |

sHAS-BLED=simplified HAS-BLED; CRNMB=clinically relevant non-major bleeding; OR=odds ratio; CI=confidence interval

**Table 3.** Sensitivity, specificity, PPV, NPV, and AUC of sHAS-BLED and cHAS-BLED scores

| Scoring system | Sensitivity | Specificity | PPV | NPV | AUC (95%CI) |
|---|---|---|---|---|---|
| sHAS-BLED | 53.57% | 69.51% | 37.50% | 81.43% | 0.65 (0.53 to 0.77) |
| cHAS-BLED | 50.00% | 84.15% | 51.85% | 83.13% | 0.67 (0.55 to 0.80) |

PPV=positive predictive value; NPV=negative predictive value; AUC=area under the curve; CI=confidence interval

INR in cHAS-BLED score as TTR of less than 70%, while cHAS-BLED score in European guidelines was defined as TTR of less than 60%[6]. Second, that trial did not demonstrate whether sHAS-BLED could predict bleeding risk in AF patients.

The present trial was conducted to compare sHAS-BLED and cHAS-BLED scores in bleeding risk prediction. The labile INR in cHAS-BLED score was defined as TTR of less than 60% following the European clinical practice guideline[6]. The sHAS-BLED score had lower specificity and PPV while comparable sensitivity and NPV compared with cHAS-BLED score. However, the sHAS-BLED and cHAS-BLED scores had comparable discrimination performances that were demonstrated with the c-statistics of 0.65 and 0.67, respectively. The lower specificity and PPV in sHAS-BLED score may be from the substitution of labile INR with SAMe-$TT_2R_2$ score because previous contemporary trial has shown that SAMe-$TT_2R_2$ score of 3 or more predicted mean TTR of 65% or less in external validation cohort[7] while labile INR in cHAS-BLED score is defined as TTR less than 60%.

Additionally, the sHAS-BLED score was studied to predict bleeding risk by comparing patients with score of 3 or more with those with score of less than 3. Those with sHAS-BLED score of 3 or more had more total bleeding events than those with score of less than 3 with statistical significance. However, those score of 3 or more had a trend in more major bleeding or CRNMB and minor bleeding events, with no statistical significance due to low event rate.

However, the present study had some limitations. First, this was a retrospective study. There may be some missing data leading to lower bleeding event rate than expected. Second, there were few AF patients in the present study compared with the contemporary risk score trials. However, the present trial was the first study that revealed the use of sHAS-BLED score for bleeding risk prediction in AF patients. Finally, the present study recruited only Thai AF patients leading to limit the generalizability of other Asian or Caucasian patients. Nevertheless, this score had more advantage than cHAS-BLED score because the present study improved the convenient use of HAS-BLED score by using SAMe-$TT_2R_2$ as substitute for labile INR with no need of TTR calculating by using Rosendaal method[16].

## Conclusion

The sHAS-BLED score can be used for bleeding risk prediction in anticoagulated AF patients compared with cHAS-BLED score.

## What is already known on this topic?

The conventional HAS-BLED score is recommended for predicting the bleeding events in AF patients receiving warfarin.

## What this study adds?

This study has shown that simplified HAS-BLED score can be used to predict the bleeding events in Thai AF patients receiving warfarin.

## Conflicts of interest

The author declares no conflicts of interest for this article.

## References


1. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. Arch Intern Med 1994;154:1449-57.
2. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2019;74:104-32.
3. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37:2893-962.
4. Lip GYH, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B, et al. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report.

Chest 2018;154:1121-201.
5. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. 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;138:1093-100.
6. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;31:2369-429.
7. Apostolakis S, Sullivan RM, Olshansky B, Lip GYH. Factors affecting quality of anticoagulation control among patients with atrial fibrillation on warfarin: the SAMe-$TT_2R_2$ score. Chest 2013;144:1555-63.
8. Bernaitis N, Ching CK, Chen L, Hon JS, Teo SC, Davey AK, et al. The sex, age, medical history, treatment, tobacco use, race risk (SAMe TT(2)R(2)) score predicts warfarin control in a Singaporean population. J Stroke Cerebrovasc Dis 2017;26:64-9.
9. Chan PH, Hai JJ, Chan EW, Li WH, Tse HF, Wong IC, et al. Use of the SAMe-$TT_2R_2$ score to predict good anticoagulation control with warfarin in Chinese patients with atrial fibrillation: relationship to ischemic stroke incidence. PLoS One 2016;11:e0150674.
10. Lip GYH, Haguenoer K, Saint-Etienne C, Fauchier L. Relationship of the SAMe-$TT_2R_2$ score to poor-quality anticoagulation, stroke, clinically relevant bleeding, and mortality in patients with atrial fibrillation. Chest 2014;146:719-26.
11. Methavigul K. Proportion of Thai patients with atrial fibrillation receiving warfarin with labile INR in each group of SAMeTT2R2 score. J Med Assoc Thai 2018;101:189-93.
12. Methavigul K. Use of SAMe-$TT_2R_2$ score to predict the quality of anticoagulation control in patients with atrial fibrillation receiving warfarin in Thailand. J Med Assoc Thai 2020;103:548-52.
13. Proietti M, Lane DA, Lip GY. Relation of the SAMe-$TT_2R_2$ score to quality of anticoagulation control and thromboembolic events in atrial fibrillation patients: Observations from the SPORTIF trials. Int J Cardiol 2016;216:168-72.
14. Methavigul K, Methavigul R. Use of simplified HAS-BLED score in patients with atrial fibrillation receiving warfarin. J Arrhythm 2019;35:711-5.
15. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost 2005;3:692-4.
16. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost 1993;69:236-9.