A Standardized Bleeding Risk Score Aligns Anticoagulation Choices with Current Evidence

Arielle S. Berger, MD,* Andrew S. Dunn, MD, MPH,† and Amy S. Kelley, MD, MSHS‡§

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the United States. Its prevalence increases with age, occurring in 18% of those aged more than 85 years.1,2 The stroke risk associated with AF is on average 4% per year (ranging from <1% to >20% depending on age and the number of risk factors), and strokes due to AF are associated with higher morbidity and mortality compared to non-AF-related strokes.3,4 Oral anticoagulation (OAC) can decrease the risk of stroke by 60%; however, the bleeding complications associated with OAC in AF increase with age as well, making the decision of whether to anticoagulate a common clinical conundrum.5 Fewer than 60% of ideal candidates are anticoagulated.5–7 Patient-, physician- and health care system-related factors have been identified as barriers to appropriate OAC.5 Physician-related barriers include knowledge gaps among physicians of the relative risks and benefits of OAC, lack of familiarity with clinical guidelines, and personal experience with poor outcomes.3 Few studies to date have examined interventions to overcome physician-related barriers. Numerous clinical prediction rules have been developed to assist with decision making in patients with AF. The CHADS2 score (Congestive heart failure, Hypertension, Age ≥75, Diabetes mellitus, Stroke × 2 points), which can distinguish between patients with high and low risk of stroke, has been widely validated and adopted.3 Recently, clinical prediction rules have been developed to assess the risk of major bleeding in patients with AF who are treated with OAC. The HAS-BLED score (Hypertension, Abnormal liver or renal function, Stroke, Bleeding history, Labile INR, Elderly, Drugs/alcohol), developed prospectively in a European cohort, has been externally validated in multiple settings to predict major bleeding complications with moderate-to-good predictive accuracy.8–10

This study sought to assess whether use of the HAS-BLED score in clinical decision making will lead to more appropriate OAC choices. To our knowledge, this is the first study assessing the impact of using HAS-BLED on clinical decision making. We hypothesized that use of HAS-BLED will align OAC decisions with best available evidence and improve rates of appropriate OAC.

METHODS

We recruited physicians from a large urban academic medical center to participate in a survey. Physicians in the divisions of general internal medicine, hospital medicine, geriatrics, cardiology, and palliative medicine at Mount Sinai Medical Center in New York City were eligible for the study. Eligible participants were randomly assigned to the intervention or control groups using a random number generator. An email introducing the study was sent to each eligible participant with a link to the assigned version (i.e., intervention or control) of the online survey. To encourage participation, participants were given the opportunity to enter a raffle to win one of four US$25 gift cards after completing the survey. A reminder email was sent to the entire list of eligible physicians 2 weeks later.

The Institutional Review Board approved the study, and informed consent was obtained electronically at the start of the survey. The survey was comprised of four vignettes highlighting common, complex scenarios of older patients with new-onset atrial fibrillation, including factors such as alcohol use, poor medication adherence, age above 85 years, risk of falls, multimorbidity, and additional stroke risk factors such as coronary artery disease. Respondents were asked whether they would recommend oral anticoagulation or not for the patient in each vignette. Oral anticoagulants were defined as warfarin, dabigatran, or rivaroxaban. Aspirin was not considered an anticoagulant, and apixaban was not marketed in the United States at the time of the study. Subjects were also asked to estimate the annual risk of stroke as a percentage from 0 to 100 for the patient in each vignette.

From the *Department of Medicine, Mount Sinai and University Health Network Hospitals, Toronto, ON, Canada; †Department of Medicine, Mount Sinai Hospital, New York, NY; ‡Brookdale Department of Geriatrics and Palliative Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; and §Geriatric Research Education and Clinical Centers, James J Peters VA Medical Center, Bronx, New York, NY

This work was presented in poster form at the American Geriatrics Society Annual Scientific Meeting in Grapevine, Texas on May 3, 2013.
Reprints: Arielle S. Berger, MD, 550 University Avenue, 5–113, Toronto, ON MSG 2A2, Canada. E-mail: arielle.berger@uhn.ca

Copyright © 2014 by Lippincott Williams & Wilkins. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

ISSN: 1003-0117/14/1303-0109
DOI: 10.1097/HPC.000000000000017

OBJECTIVES: Atrial fibrillation (AF), the most common arrhythmia in elderly patients, accounts for 15% of strokes. Oral anticoagulation (OAC) can reduce the risk of stroke by 60% but is underprescribed. The HAS-BLED score (Hypertension, Abnormal renal or liver function, Stroke, Bleeding, Labile INR, Elderly, Drugs) can predict OAC bleeding complications. The authors hypothesized that use of HAS-BLED can help align decision making with current evidence.

METHODS: The authors developed a survey with four clinical vignettes designed to highlight the complexity in deciding whether to anticoagulate elderly patients with AF. Physicians were randomly assigned to receive the survey either including the HAS-BLED score and the estimated annual risk of bleeding (intervention) or without (control). Following each vignette, participants were asked: (1) whether they would recommend OAC and (2) to estimate the risk of bleeding and stroke. The “appropriate” anticoagulation decision was defined as the choice that minimized the risk of stroke and major bleeding.

RESULTS: A total of 203 physicians were recruited for the survey, with 55 responses obtained (27%). Physicians who were given the HAS-BLED score were 18% more likely to choose appropriate anticoagulation (74% vs. 56%, P < .05). The HAS-BLED score assisted physicians in both choosing to anticoagulate when appropriate and not to anticoagulate when the risk of bleeding outweighed the benefit. Overall, physicians were poor at estimating the risk of stroke (42% correct) and major bleeding (31% correct).

CONCLUSIONS: Presentation of the HAS-BLED score led to an 18% improvement in appropriate OAC choices. Future study should evaluate incorporation of HAS-BLED use in real-time clinical situations.

Key Words: Oral anticoagulation, atrial fibrillation, stroke, major bleeding, HAS-BLED

(Crit Pathways in Cardiol 2014;13: 109–113)
The intervention group was provided with: (1) an introduction to the HAS-BLED clinical prediction rule and scoring system and (2) the HAS-BLED score and annual risk of major bleeding associated with each vignette. The control group did not receive this information and was instead asked to estimate the annual risk of bleeding as a percentage from 0 to 100. The survey did not indicate a stroke-risk score in either the intervention or control version of the survey. Additional questions assessed the respondents’ comfort in making these clinical decisions. Baseline demographic data were collected including gender, specialty, and years of clinical experience of each participating physician.

The primary outcome was the proportion of appropriate OAC choices, compared between the intervention and control groups. The appropriate treatment choice was defined as the treatment that would provide a net clinical benefit by minimizing the overall risk of strokes and major bleeding events. The following definition for net clinical benefit was used:

\[
\text{Net Clinical Benefit} = \text{Stroke}_{\text{off OAC}} - (\text{Stroke}_{\text{on OAC}} + \text{Major Bleeding}_{\text{on OAC}}).
\]

Stroke risk on OAC was calculated as a 60% reduction of the stroke risk off OAC. For example, consider a scenario in which withholding OAC was associated with an annual stroke rate of 5.0% and the major bleeding rate on OAC was 2.0%. The total predicted event rate off OAC would be 5.0%, and the total predicted event rate on OAC was calculated as a stroke rate of 2.0% (i.e., a 60% reduction in the baseline risk) plus the major bleeding rate on OAC of 2.0%, for a total rate of 4.0%. Hence, the correct treatment choice would be to administer OAC.

Given the dramatic difference in the consequences of intracranial bleeding and nonintracranial bleeding, other studies examining the net clinical benefit of OAC have focused on the risk of intracranial hemorrhage (ICH) caused by OAC rather than all major bleeding. As clinicians may be primarily concerned with the increased risk of ICH, we performed a sensitivity analysis using an alternate definition of net clinical benefit as follows:

\[
\text{Net Clinical Benefit} = \text{Stroke}_{\text{off OAC}} - (\text{Stroke}_{\text{on OAC}} + \text{ICH}_{\text{on OAC}}).
\]

We assessed physicians’ accuracy in estimating the annual risk of stroke and major bleeding, as poor estimation may lead to selecting an anticoagulation strategy that does not minimize the risk of adverse events. The CHADS2 and CHA2DS2-VASc (Congestive heart failure, Hypertension, Age ≥75 × 2 points, Diabetes mellitus, Stroke × 2 points, Vascular disease, Age 65–75 × 1 point, Sex category [female]) scores were calculated for the patient in each vignette. The range of annual stroke risk associated with those scores was used to define the correct stroke risk. For example, in a patient with a CHADS2 score of 1, which corresponds to a 2% annual risk of stroke, and CHA2DS2-VASc score of 4, which corresponds to a 3% risk of stroke, the correct risk of stroke was defined as the range of 2–3% per year. The same methodology was used to define the correct annual risk of major bleeding. The HAS-BLED and ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation Study) scores were calculated for the patient in each vignette. These bleeding risk scores were chosen because they have the best clinical accuracy for predicting major bleeding. The correct annual risk of major bleeding was defined by the range predicted by the HAS-BLED and ATRIA risk scores.

Proportions of appropriate OAC choices and correct annual stroke risk estimates were compared between intervention and control groups using Chi-squared and Fisher’s exact tests.

**RESULTS**

A total of 203 physicians were recruited for the study. Fifty-five (27%) participants responded. There were no significant differences in demographic characteristics between intervention and control groups (Table 1). Geriatricians represented the largest proportion of the respondents (49%) and had the highest response rate (55%). A variety of levels of training, including fellows-in-training, early-career, and experienced clinicians participated. Characteristics of the four vignettes are described in Table 2.

Physicians who were given the HAS-BLED score (intervention group) were 18% more likely to make the appropriate anticoagulation choice (74% vs. 56%, \( P = 0.009 \)) (Fig. 1). The HAS-BLED score assisted physicians in both choosing to anticoagulate when appropriate and not to anticoagulate when the risk of bleeding outweighed the benefit (Fig. 2). Each vignette highlighted a unique clinical consideration. Vignette A described an elderly patient with multiple comorbidities, including coronary and peripheral arterial disease limiting ambulation. This patient’s CHADS2 score, 1 (corresponding to a 2.8% annual risk of stroke, classified as intermediate risk) and CHA2DS2-VASc score is 4 (3% annual risk of stroke, high risk). The most recent guidelines recommend treatment with OAC for such a patient. All respondents (27/27) who were given the HAS-BLED score (which indicated a low risk of bleeding) chose to anticoagulate this patient, compared to only 22 of 26 (85%) in the control group (\( P = 0.05 \)). In this scenario, HAS-BLED significantly improved the likelihood that clinicians would choose to anticoagulate an appropriate candidate.

Vignette B highlighted treatment of AF in the oldest old. Based on risk factors, this patient would be at high risk for stroke with a CHADS2 score of 2 (4% annual risk of stroke) and low risk for bleeding with a HAS-BLED score of 1 (1% annual risk of major bleeding). Despite this, respondents in both groups were split regarding recommending OAC, with only 14 of 27 respondents in the intervention group and 14 of 26 in the control group recommending OAC. In this case the HAS-BLED score did not influence treatment decisions. Geriatricians showed a trend toward being more likely to choose OAC in this vignette than other specialists (19 of 29 geriatricians recommended OAC vs. only 9 of 33 nongeriatricians, \( P = 0.058 \)), though across all four vignettes geriatricians were not more likely to recommend OAC (59% vs. 56%).

Vignette C highlighted a patient with high bleeding risk, estimated at 9% per year (HAS-BLED score is 4). In this case, we found that the intervention group was much less likely to recommend OAC than the control group (5/27 vs. 17/26, \( P = 0.002 \)). Here, the HAS-BLED score helped physicians identify a patient at very high risk for bleeding and avoid treatment with OAC.

Vignette D described a patient with poor medication adherence and alcohol abuse, where the event rate on OAC was slightly

| TABLE 1. Baseline Characteristics |
|----------------------------------|
| Characteristic                  | Intervention | Control |
|---------------------------------|--------------|---------|
| Recruited                       | 99           | 104     |
| Responses                       | 27 (27%)     | 27 (26%)|
| Sex                             |              |         |
| Female                          | 17           | 17      |
| Specialty                       |              |         |
| Internal medicine               | 8            | 8       |
| Geriatrics                      | 14           | 15      |
| Cardiology                      | 4            | 3       |
| Palliative care                 | 4            | 4       |
| Experience                      |              |         |
| In fellowship training          | 2            | 8       |
| Completed training ≤5 years     | 9            | 5       |
| Completed training >5 years     | 15           | 13      |

\( * P < 0.05 \)
Risk Score Improves Anticoagulation Choices

**TABLE 2. Description of Vignettes**

| Vignette | Risk of stroke (% per year) without OAC | Risk of stroke (% per year) on OAC* | Risk of bleeding (% per year) on OAC | “Appropriate” treatment Recommendation |
|----------|----------------------------------------|-------------------------------------|-------------------------------------|----------------------------------------|
| A: 80-year-old female with new AF, CAD, PVD, OA, exercise tolerance limited to 2 blocks; CHA2DS2-VASc = 4; HAS-BLED = 1 | 3.0% | 1.2% | 1.0% | Treat with OAC |
| B: 95-year-old male with new AF, a mild mechanical fall, DM2, mild dementia; CHA2DS2-VASc = 3; HAS-BLED = 1 | 2.0% | 0.8% | 1.0% | Treat with OAC |
| C: 75-year-old male with new AF, HTN, and CKD4. Remote history of duodenal ulcer hemorrhage; CHA2DS2-VASc = 3; HAS-BLED = 4 | 2.0% | 0.8% | 9.0% | Do not treat with OAC |
| D: 60-year-old female with new AF, alcoholic, uncontrolled HTN, PAD, on aspirin, poor adherence to medications; CHA2DS2-VASc = 3; HAS-BLED = 3 | 2.0% | 0.8% | 4.0% | Do not treat with OAC |

CAD, coronary artery disease; CHA2DS2-VASc, Congestive heart failure, Hypertension, Age >75 × 2 points, Diabetes mellitus, Stroke × 2 points, Vascular disease, Age 65–75 × 1 point, Sex category (female); CKD4, chronic kidney disease stage 4; F, female; HAS-BLED, Hypertension, Abnormal renal or liver function, Stroke, Bleeding, Labile International normalized ratio (INR), Elderly, Drugs; HTN, hypertension; M, male; OA, osteoarthritis; OAC, oral anticoagulation; PAD, peripheral arterial disease

*Defined as the risk of stroke per year without OAC × 0.4 (a 60% relative risk reduction)*

DISCUSSION

This study suggests that incorporating the HAS-BLED clinical prediction rule into clinical decision making may improve the rate of appropriate OAC for older adults with atrial fibrillation. In this vignette-based survey, we found that use of HAS-BLED improved the likelihood to make the appropriate decision regarding anticoagulating complex patients with atrial fibrillation by 18%. We also investigated a possible source of inappropriate decision making and found that physicians were frequently incorrect at estimating the risks of stroke and major bleeding. This knowledge gap likely contributes to the undertreatment of patients with atrial fibrillation in clinical practice and could potentially be ameliorated through the use of validated risk scores.

The main limitations of this study are the small sample size and examination of physicians at a single academic medical center in the United States. Our response rate was low (27%), though similar to other studies surveying physicians. Geriatricians were more likely to participate in the survey compared to other specialists. It is plausible that clinicians more comfortable with management of atrial fibrillation in the elderly patients were more likely to respond to our survey. The number of more experienced physicians was higher in the intervention group than in the control group, and although this difference did not reach statistical significance (P = 0.08), it could be a possible source of bias in the results. However, both these biases would strengthen our findings as they would suggest that even those most comfortable with AF and OAC have significant knowledge gaps. Despite our low numbers, our survey did include respondents from a variety of specialties and levels of experience.

The finding from our secondary analysis focusing on the risk of intracranial bleeding rather than all major hemorrhage indicates that clinicians and patients placing low weight on nonintracranial bleeding events may not find the HAS-BLED score clinically beneficial. It is also important to note that both the HAS-BLED and ATRIA...
risk scores for predicting major bleeding were developed in populations using only warfarin for OAC. Given that the bleeding-risk profiles with new oral anticoagulants vary somewhat from warfarin, it may not be appropriate to directly apply the HAS-BLED scores to those patients.\textsuperscript{18} We show that use of the HAS-BLED score has the potential to improve clinical decision making and align medical choices with the best available evidence; however, clinical prediction rules do pose certain challenges and limitations. In vignette D, we found that although the risk of adverse events on OAC was greater than the risk of stroke off OAC, the intervention group recommended OAC at similar rates to the control group (37% vs. 48%); presentation of the moderately elevated HAS-BLED score did not significantly sway clinicians to avoid OAC. This may stem from a concern among clinicians that various risk scores cannot simply be compared numerically, as the morbidity associated with bleeding compared to stroke is very different. Interestingly, in Vignette C, where the bleeding risk is more than double the stroke risk, presentation of HAS-BLED did impact decision making and led to a lower rate of anticoagulation in the intervention group. These results highlight the difficulty in determining the correct treatment choice when bleeding risk only slightly outweighs stroke risk.

Our results shed light on a second group of patients for whom there is great uncertainty about appropriate OAC choices and the limitations of the HAS-BLED clinical prediction rule: the oldest old. Vignette B describes a patient with a relatively high stroke risk and a low bleeding risk. Although use of the HAS-BLED score may be expected to encourage clinicians to anticoagulate such a patient, we found no impact of presentation of the HAS-BLED score in this scenario. As clinical trials generally underrepresent elderly patients,\textsuperscript{19} perhaps clinicians are not applying these tools to their patients as they feel the evidence does not accurately reflect the population they are treating. Interestingly, we found a trend toward geriatricians being more likely to offer OAC to the patient in Vignette B compared to other specialists. Perhaps this is due to an education bias among geriatricians who are more familiar with treating elderly patients with AF and aware of the evidence suggesting that falls alone should not be a deterrent to anticoagulating patients at high risk for stroke.\textsuperscript{20}

The implications of this study are threefold. First, our vignette-based survey has shown that use of HAS-BLED leads to more appropriate decisions regarding the use of OAC in the setting of a survey. Thus, prospective studies are needed to evaluate the impact of HAS-BLED in clinical practice. Second, despite the fact that atrial fibrillation is one of the most common cardiac diseases encountered in general medicine, geriatrics, and cardiology, there remain large knowledge gaps about the actual risk of adverse outcomes associated with various treatment options. Education of trainees and practitioners about risk assessment for both stroke and major bleeding is needed so that clinicians can continue to make informed decisions and counsel patients appropriately. Third, the HAS-BLED score had less impact in scenarios for which there is poor consensus in the medical

FIGURE 2. Effect of HAS-BLED according to vignette.
community about appropriate treatment: those with moderately elevated bleeding risk and the oldest old. More evidence specifically describing the outcomes of elderly patients with AF is needed to answer some of the most challenging decisions we face in attempting to prevent strokes while following the mandate to “First do no harm.”

DISCLOSURES
Conflicts of Interest and Sources of Funding: ASD received medications from Desai Pharmaceuticals for use in an RCT not related to this manuscript. ASK is supported by the American Federation for Aging Research and National Institute on Aging (1K23AG040774-01A1). For ASB none were declared.

ACKNOWLEDGMENTS
Dr. Berger received support for this research while serving as a clinical geriatrics fellow in the Brookdale Department of Geriatrics and Palliative Medicine at Icahn School of Medicine at Mount Sinai, New York. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES
1. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Arch Intern Med. 1995;155:469–473.
2. Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006;27:949–953.
3. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864–2870.
4. Romero J.R, Morris J, Pikula A. Stroke prevention: modifying risk factors. Ther Adv Cardiovasc Dis. 2008;2:287–303.
5. Bungard TJ, Ghali WA, Teo KK, McAlister FA, Tsuyuki RT. Why do patients with atrial fibrillation not receive warfarin? Arch Intern Med. 2000;160:41–46.
6. Fang MC, Stafford RS, Ruskin JN, Singer DE. National trends in antithrombotic and antithrombotic medication use in atrial fibrillation. Arch Intern Med. 2004;164:55–60.
7. Ogilvie IM, Newton N, Welner SA, Cowell W, Lip GY. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. Am J Med. 2010;123:638–645.e4.
8. 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;138:1093–1100.
9. Olesen JB, Lip GY, Hansen PB, et al. Bleeding risk in ‘real world’ patients with atrial fibrillation: comparison of two established bleeding prediction schemes in a nationwide cohort. J Thromb Haemost. 2011;9:1460–1467.
10. Roldán V, Marín F, Fernández H, et al. Predictive value of the HAS-BLED and ATRIA bleeding scores for the risk of serious bleeding in a “real-world” population with atrial fibrillation receiving anticoagulant therapy. Chest. 2013;143:179–184.
11. Friberg L, Rosenqvist M, Lip GY. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish atrial fibrillation cohort study. Circulation. 2012;125:2298–2307.
12. Singer DE, Chang Y, Fang MC, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med. 2009;151:297–305.
13. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Circulation. 2010;120:263–272.
14. Apostolakis S, Lane DA, Guo Y, Buller H, Lip GY. Performance of the HEMORR 2 HAGES, ATRIA, and HAS-BLED bleeding risk-prediction scores in nonwarfarin anticoagulated atrial fibrillation patients. J Am Coll Cardiol. 2013;61:386–387.
15. You JJ, Singer DE, Howard PA, et al; American College of Chest Physicians. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e531S–e575S.
16. January CT, Wann LS, Alpert JS, et al. 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 Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014 pii: S0735–7597.
17. VanGeest JB, Johnson TP, Welch VL. Methodologies for improving response rates in surveys of physicians: a systematic review. Eval Health Prof. 2007;30:303–321.
18. Dentali F, Riva N, Crowther M, Turpie AG, Lip GY, Ageno W. Efficacy and safety of the novel oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of the literature. Circulation. 2012;126:2381–2391.
19. Konrat C, Boutron I, Trinquart L, Auleye GR, Ricordeau P, Ravaud P. Underrepresentation of elderly people in randomised controlled trials. The example of trials of 4 widely prescribed drugs. PLoS One. 2012;7:e33559.
20. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk for falls. Arch Intern Med. 1999;159:677–685.

* Question was not posed to control group as they were not exposed to the HAS-BLED score

FIGURE 3. Comfort with decision making.