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The HAS-BLED Score Has Better Prediction Accuracy for Major Bleeding Than $CHADS_2$ or CHA_2DS_2-VASc Scores in Anticoagulated Patients With Atrial Fibrillation

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Objectives The aim of this study was to test the hypothesis that a specific bleeding risk score, HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly), was better at predicting major bleeding compared with $CHADS_2$ (congestive heart failure, hypertension, 75 years of age or older, diabetes mellitus, and previous stroke or transient ischemic attack) and CHA_2DS_2-VASc (congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female) in anticoagulated atrial fibrillation (AF) patients.

Background The $CHADS_2$ and CHA_2DS_2-VASc scores are well-validated stroke risk prediction scores for AF, but are also associated with increased bleeding and mortality.

Methods We recruited 1,370 consecutive AF patients (49% male; median age, 76 years) receiving oral anticoagulation therapy from our outpatient anticoagulation clinic, all of whom were receiving acenocoumarol and had an international normalized ratio between 2.0 and 3.0 during the preceding 6 months. During follow-up, major bleeding events were identified by the 2005 International Society on Thrombosis and Haemostasis criteria.
Model performance was evaluated by calculating the C-statistic, and the improvement in predictive accuracy was evaluated by calculating the net reclassification improvement and integrated discrimination improvement.

Results After a median follow-up of 996 (range, 802 to 1,254) days, 114 patients (3.0%/year) presented with a major bleeding event; 31 of these events were intracranial hemorrhages (0.8%/year). Based on the C-statistic, HAS-BLED had a model performance superior to that of both $CHADS_2$ and CHA_2DS_2-VASc (both $p < 0.001$).
Both net reclassification improvement and integrated discrimination improvement analyses also show that HAS-BLED was more accurately associated with major bleeding compared with $CHADS_2$ and CHA_2DS_2-VASc scores.

Conclusions In anticoagulated AF patients, a validated specific bleeding risk score, HAS-BLED, should be used for assessing major bleeding. The practice of using $CHADS_2$ and CHA_2DS_2-VASc as a measure of high bleeding risk should be discouraged, given its inferior predictive performance compared with the HAS-BLED score. (J Am Coll Cardiol 2013;62:2199–204) © 2013 by the American College of Cardiology Foundation

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Abbreviations and Acronyms

AF = atrial fibrillation

$CHADS_2$ = congestive heart failure, hypertension, 75 years of age or older, diabetes mellitus, and previous stroke or transient ischemic attack

CHA_2DS_2-VASc = congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female

CI = confidence interval

HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly

HR = hazard ratio

IDI = integrated discrimination improvement

INR = international normalized ratio

NRI = net reclassification improvement

OAC = oral anticoagulation

VKA = vitamin K antagonist

Oral anticoagulation (OAC) is highly effective in reducing the risk of stroke in atrial fibrillation (AF) patients (1). Decisions on thromboprophylaxis have been based on stroke risk, as assessed by different stroke risk stratification schemes (2), such as the $CHADS_2$ (congestive heart failure, hypertension, 75 years of age or older, diabetes mellitus, and previous stroke or transient ischemic attack) score (3). More recently, the CHA_2DS_2-VASc (congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, 65 to 74 years of age, female) score has been used in guidelines, with particular focus on the initial identification of "truly low risk" patients as the initial decision-making step (2,4,5).

Stroke risk and bleeding risk are closely related, and the $CHADS_2$ score closely correlates with bleeding rate (6,7). This has led to many clinicians occasionally using the $CHADS_2$ (and more recently CHA_2DS_2-VASc) as an indicator of bleeding risk, which could lead to the low use of OAC in those with high $CHADS_2$ (or CHA_2DS_2-VASc) scores (8–10). In some prescribing recommendations for the novel oral anticoagulants, the lower dose of, for example, dabigatran is recommended at high bleeding risk as quantified by a high $CHADS_2$ score (11,12).

Specific bleeding risk scores are available for patients with AF (13), and the HAS-BLED score is now recommended in European and Canadian AF guidelines to estimate major bleeding risk in anticoagulated AF patients (5,13–15). HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly) has been shown to perform better than other bleeding risk scores (such as HEMORR2HAGES [Hepatic or Renal Disease, Ethanol Abuse, Malignancy, Older Age, Reduced Platelet Count or Function, Re-Bleeding, Hypertension, Anemia, Genetic Factors, Excessive Fall Risk and Stroke], ATRIA [Anticoagulation and Risk Factors in Atrial Fibrillation]) for predicting serious bleeding in vitamin K antagonist (VKA) and non-VKA anticoagulated clinical trial cohorts of AF patients (16), as well as real-world clinical practice (17,18). HAS-BLED is also the only risk score predictive of intracranial bleeding in AF (16) and non-AF (19) patients. Also, HAS-BLED has been related to major bleeding during bridging (20) and percutaneous coronary interventions (21,22) in both AF and non-AF cohorts.

In the present study, we tested the hypothesis that a specific bleeding risk score, HAS-BLED, was better at predicting major bleeding compared with $CHADS_2$ and CHA_2DS_2-VASc in anticoagulated AF patients.

Methods

Patients. We recruited consecutive patients with permanent or paroxysmal AF receiving OAC therapy from our outpatient anticoagulation clinic. We studied patients who were entered into our anticoagulation clinic database in 2007 and the first trimester of 2008. The various clinical parameters needed to calculate the HAS-BLED and CHA_2DS_2-VASc scores were available on our database, and, thus, the various scores were applied retrospectively to the cohort for the present analysis.

All patients were receiving anticoagulation therapy with acenocoumarol and consistently achieved an international normalized ratio (INR) between 2.0 and 3.0 during the previous 6 months of clinic visits. Patients with prosthetic heart valves, acute coronary syndrome, stroke (ischemic or embolic), valvular AF, or any hemodynamic instability as well as patients who had hospital admission or surgical intervention in the preceding 6 months were excluded from the study. A complete medical history was recorded. Follow-up was performed through visits to the anticoagulation clinic.

The HAS-BLED bleeding risk score (14) was calculated as a measure of baseline bleeding risk, as the result of adding 1 point to hypertension, abnormal renal/liver function (1 point each), stroke, bleeding history or predisposition, labile INR, elderly (65 years of age and older), and drugs/alcohol concomitantly (1 point for each one). Based on our inclusion criteria at entry, labile INR was quantified as 0 in every patient.

Baseline stroke risk was assessed using the $CHADS_2$ and CHA_2DS_2-VASc scores (3,4).

Major bleeding events were defined by the 2005 International Society on Thrombosis and Haemostasis criteria (23).

Statistical analysis. Continuous variables were tested for normality by the Kolmogorov-Smirnov test. Continuous variables are presented as a mean ± SD or median (interquartile range, as appropriate, and categorical variables as a percentage. Cox models were used to determine the associations between clinical scores and bleeding as well as and mortality.

Model performance was evaluated by calculating C-statistic, and the improvement in predictive accuracy was evaluated by calculating the net reclassification improvement (NRI) and integrated discrimination improvement (IDI), as described by Pencina et al. (24), where the categories of probability for events are defined based on the HAS-BLED or $CHADS_2$ or CHA_2DS_2-VASc scores. We used the method described by Hanley and McNeil (25,26) for the comparison of correlated C-statistic.