# Use of the $CHA_2DS_2$-VASc and HAS-BLED Scores to Aid Decision Making for Thromboprophylaxis in Nonvalvular Atrial Fibrillation

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# Use of the $CHA_2DS_2$-VASc and HAS-BLED Scores to Aid Decision Making for Thromboprophylaxis in Nonvalvular Atrial Fibrillation

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A 65-year-old woman with a history of myocardial infarction presented to the emergency department with palpitations. ECG on admission documented atrial fibrillation (AF), which subsequently reverted spontaneously to sinus rhythm. Echocardiogram revealed mild systolic impairment, normal left atrial size, and normal valves. Thyroid function tests were normal. She returned to the outpatient clinic 4 weeks later with a history of intermittent palpitations. Her average clinic blood pressure was 140/85 mm Hg, and the 30-day cardiac loop monitor demonstrated AF, which coincided with diary entries of symptoms of palpitations. What is the most appropriate stroke prophylaxis for this patient, given her new-onset AF?

AF increases the risk of stroke 5-fold, and anticoagulant therapy reduces the risk of stroke and all-cause mortality.[1,2] Consequently, clinical guidelines recommend stroke thromboprophylaxis among AF patients unless they are at low risk; low-risk patients are defined as those with age <65 years and lone AF.[1,2] Indeed, the risk of stroke among patients with AF is heterogeneous and depends on the presence of various stroke risk factors.[3,4]

Numerous stroke risk stratification schemas have been developed on the basis of risk factors identified from nonwarfarin arms of clinical trials, cohort studies, and consensus expert panels. These schemas vary in their complexity and the number of risk factors they include and have conventionally categorized AF patients into low, moderate, and high risk. Traditionally, guidelines have recommended aspirin or antiplatelet therapy for those at low risk of stroke and oral anticoagulation (OAC) for those at high risk, whereas individuals at moderate risk have the option of receiving either aspirin or oral anticoagulation. To determine the most appropriate antithrombotic therapy for each patient, the individual risk of stroke should be assessed.

Systematic reviews[3–5] demonstrate that the main risk factors for stroke in patients with AF are previous stroke or transient ischemic attack, increasing age, hypertension, heart failure, and diabetes mellitus (Table 1). The widely used $CHADS_2$ score[6] (Congestive Heart Failure, Hypertension, Age ≥75 Years, Diabetes Mellitus [1 point for presence of each], and Stroke/TIA [2 points]; scores range from 0 to 6) was derived from the risk factors obtained from the original (now historical) data sets from the AF Investigators and the Stroke Prevention in AF 1 trial. Of note, the historical trials randomized <10% of the patients who were screened, and many risk factors were inconsistently defined or systematically recorded.

**Table 1. Risks Factors for Stroke in Nonvalvular Atrial Fibrillation Patients**

| |
|---|
| Previous stroke |
| Transient ischemic attack |
| Previous thromboembolism |
| Age |
| Hypertension |
| Heart failure |
| Diabetes mellitus |
| Female sex |
| Vascular disease |
| Coronary or peripheral artery disease |

Over the last decade, major developments have led to significant

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changes in the antithrombotic management of patients with AF. First, new data have emerged on what were previously referred to as less well validated risk factors for stroke, namely female sex, age of 65 to 74 years, and vascular disease.[7,8] Second, cohort studies have demonstrated the benefit of OAC over aspirin in terms of stroke reduction and mortality, even in patients at so-called moderate risk (eg, $CHADS_2$ score of 1).[1] Third, the benefit of aspirin for stroke prophylaxis in AF has been questioned.[9] Finally, 3 large randomized, controlled trials of novel OAC drugs have demonstrated noninferiority—in some cases, superiority—compared with warfarin in terms of both efficacy and safety. Given that stroke risk in AF is a continuum, a risk factor–based approach to risk assessment has resulted in a paradigm shift that now focuses on better identification of truly low-risk patients who do not need any antithrombotic therapy, whereas those with ≥1 stroke risk factors can be considered for effective stroke prevention therapy, which is essentially OAC, whether with well-controlled dose-adjusted warfarin or one of the new agents.

## Use of $CHA_2DS_2$-VASc to Assess Stroke Risk

Although simple, the $CHADS_2$ score does not include many common stroke risk factors, and its limitations have recently been highlighted.[10,11] Even patients classified as low risk by $CHADS_2$ in its original validation study have a stroke rate of 1.9%/y,[6] which is close to the criterion of a cardiovascular event rate of 20% over 10 years for primary prevention strategies (eg, the use of statins). A recent analysis also confirms that patients with a $CHADS_2$ score of 0 were not all low risk, and anticoagulation decisions based simply on a $CHADS_2$ score of 0 (the category recommended to have no antithrombotic therapy or aspirin in some guidelines) may be insufficient to avoid stroke/thromboembolism in patients with AF.[12]

**Table 2. Assessment of Stroke ($CHA_2DS_2$-VASc)[14] and Bleeding Risk (HAS-BLED)[15] in Atrial Fibrillation Patients**

| $CHA_2DS_2$-VASc | Score | HAS-BLED | Score |
|---|---|---|---|
| Congestive heart failure | 1 | Hypertension (systolic blood pressure >160 mm Hg) | 1 |
| Hypertension | 1 | Abnormal renal and liver function* (1 point each) | 1 or 2 |
| Age ≥75 y | 2 | Stroke | 1 |
| Diabetes mellitus | 1 | Bleeding tendency/predisposition* | 1 |
| Stroke/TIA/TE | 2 | Labile INRs (if on warfarin)* | 1 |
| Vascular disease (prior MI, PAD, or aortic plaque) | 1 | Elderly (eg, age >65 y) | 1 |
| | | Drugs or alcohol (1 point each)* | 1 or 2 |
| Aged 65 to 74 y | 1 | | |
| Sex category (ie, female sex) | 1 | | |
| Maximum score | 9 | Maximum score | 9 |

TIA indicates transient ischemic attack; TE, thromboembolic; INR, international normalized ratio; MI, myocardial infarction; and PAD, peripheral artery disease. $CHA_2DS_2$-VASc score of 0: recommend no antithrombotic therapy. $CHA_2DS_2$-VASc score of 1: recommend antithrombotic therapy with oral anticoagulation or antiplatelet therapy but preferably oral anticoagulation. $CHA_2DS_2$-VASc score ≥2: recommend oral anticoagulation.[2] A HAS-BLED score of ≥3 indicates that caution is warranted when prescribing oral anticoagulation and regular review is recommended.[2]

*Abnormal renal function is classified as the presence of chronic dialysis, renal transplantation, or serum creatinine ≥200 mmol/L. Abnormal liver function is defined as chronic hepatic disease (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (bilirubin 2 to 3 times the upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase 3 times the upper limit normal, etc), history of bleeding or predisposition (anemia), labile INR (ie, time in therapeutic range <60%), concomitant antiplatelets or nonsteroidal anti-inflammatory drugs, or excess alcohol.

Real-world cohort data have provided further information to inform stroke risk. Indeed, the independent predictive value of female sex, age of 65 to 74 years, and vascular disease is now evident from numerous cohorts.[7,8] In addition, a history of heart failure (the C in $CHADS_2$) is not a consistent stroke risk factor,[3,7] whereas moderate to severe systolic impairment is an independent risk factor.[13]

Given the need to be more inclusive of common stroke risk factors, the $CHA_2DS_2$-VASc score[14] has been proposed (Table 2), with scores ranging from 0 to 9. $CHA_2DS_2$-VASc acknowledges the importance of age ≥75 years as having additional weight as a single risk factor for stroke (denoted by a score of 2 points) and indicates that age is not a yes-no phenomenon because risk of stroke increases with age, particularly from 65 years of age on.[5,7] $CHA_2DS_2$-VASc also incorporates vascular disease, including myocardial infarction, aortic plaque, and peripheral vascular disease, and recognizes the increased risk of stroke among women with AF.[7]

In the original validation, $CHA_2DS_2$-VASc was compared with 7 other contemporary stroke risk stratification schemas in 1084 patients in the Euro Heart Survey on AF and demonstrated reasonable predictive ability for high-risk patients but was good at identifying low-risk patients and categorizing few patients into the moderate-risk category.[14] The $CHA_2DS_2$-VASc schema has subsequently been validated in numerous AF populations, most commonly compared with $CHADS_2$.[7,16] All studies have confirmed the ability of $CHA_2DS_2$-VASc to reliably identify 'truly low risk' patients, who could be managed with no antithrombotic therapy, as well as to predict stroke and thromboembolism in high risk patients with AF, although the C statistic varies, depending on the cohort used.

Patients who are <65 years of age with lone AF (strictly defined, irrespective of sex) have very low absolute stroke risk, and the purpose of the $CHA_2DS_2$-VASc schema is to aid in the identification of those other commonly encountered AF patients in clinical practice (ie, other than those <65

years of age and with lone AF) who are truly low risk ($CHA_2DS_2$-VASc score of 0)[17,18] who may reasonably be considered for no antithrombotic treatment. All other AF patients, those with a $CHA_2DS_2$-VASc score of ≥1, should be considered for stroke prevention, which is essentially treatment with OAC. One validation of $CHA_2DS_2$-VASc and $CHADS_2$ in a Danish nationwide cohort of 73 538 AF patients not receiving vitamin K antagonists (eg, warfarin) demonstrated that $CHA_2DS_2$-VASc performed better than $CHADS_2$ (C statistic, 0.888 [95% confidence interval, 0.875–0.900] and 0.812 [95% confidence interval, 0.796–0.827], respectively) in predicting the risk of stroke and thromboembolism.[16]

Another analysis demonstrated that patients with a $CHADS_2$ score of 0 were not all low risk when further categorized with the $CHA_2DS_2$-VASc score, with 1-year stroke/thromboembolism event rates ranging from 0.84 ($CHA_2DS_2$-VASc score=0) to 1.75 ($CHA_2DS_2$-VASc score=1), 2.69 ($CHA_2DS_2$-VASc score=2), and 3.2 ($CHA_2DS_2$-VASc score=3).[12] As mentioned, OAC decisions based simply on a $CHADS_2$ score of 0 to 1 (as in some guidelines or prescribing standards) may lead to many AF patients being provided suboptimal thromboprophylaxis and being at substantial risk of stroke.

## Why Is It Important to Risk Stratify AF Patients?

Despite the abundant evidence in favor of OAC for stroke prevention, a recent systematic review[19] investigating the current treatment practice for stroke prevention in eligible AF patients revealed ongoing underuse of OAC treatment (defined as <70% of eligible patients receiving OAC), particularly among those patients at highest risk (ie, those with a previous stroke/transient ischemic attack). Another review of antithrombotic therapy in high-risk AF patients before admission for stroke revealed that 29% of patients were not receiving any antithrombotic therapy, 31% were prescribed antiplatelet therapy, and only about one quarter of the 39% receiving warfarin (10%) achieved therapeutic international normalized ratio levels.[20] Greater efforts among physicians to prescribe OAC appropriately and to monitor antithrombotic therapy are needed if we want to reduce the incidence of stroke in AF patients and prevent the burdensome consequences of stroke for patients and their families.

Overestimation of the risk of bleeding by physicians is a key barrier to OAC prescription,[21] particularly among elderly patients, in whom aspirin is perceived as a safe and viable alternative. However, a patient-level data analysis of 12 trials comprising almost 9000 patients that assessed the effect of antithrombotic therapy on stroke prevention, serious hemorrhage, and vascular events demonstrated that although the risk of all these outcomes was greater with increasing age, OAC remained significantly protective against ischemic stroke regardless of the patient's age.[22] The relative benefit of antiplatelet therapy for protection against ischemic stroke decreased significantly as age increased, whereas the absolute benefit for OAC increased as the patients aged.[22] The risk of serious hemorrhage was relatively low, and although it increased slightly with age, there was no significant difference in hemorrhage rates between patients on aspirin and those on warfarin.[22] Thus, aspirin is not safer than warfarin in elderly people, but it is substantially less effective.

## Bleeding Risk With Antithrombotic Therapy

Many risk factors for stroke are also risk factors for bleeding on OAC[23] (see Table 3). Integral to the decision about whether to anticoagulate an AF patient is the assessment of bleeding risk, which must be undertaken on an individual basis. Until fairly recently, formal assessment of bleeding risk before the initiation of stroke thromboprophylaxis for AF patients was not recommended in clinical guidelines, attributable in part to the paucity of validated simple bleeding risk tools. A new bleeding risk score, known by the acronym HAS-BLED[15] (Table 2), is one of a number of bleeding risk tools currently available to assess AF patients (Table 4).

**Table 3. Risk Factors for Bleeding on Oral Anticoagulation**

| |
|---|
| Patient-related factors |
| Age |
| History of bleeding |
| Previous stroke |
| Anemia |
| Genetic factors |
| Sex |
| Uncontrolled hypertension |
| Renal insufficiency |
| Hepatic dysfunction |
| Malignancy |
| OAC treatment-related factors* |
| Inception vs OAC experience |
| Adherence |
| Intensity of anticoagulation (INR)* |
| Time in therapeutic range* |
| Dietary intake of vitamin K* |
| Management of OAC (self-monitoring, dedicated OAC clinic, usual care)* |
| Concomitant medications/alcohol |
| Antiplatelet drugs |
| NSAIDs |
| Other medications affecting OAC intensity |
| Excessive alcohol intake |

OAC indicates oral anticoagulants; INR, international normalized ratio; and NSAIDs, nonsteroidal antiinflammatory drugs.

*Applicable to vitamin K antagonist therapy only.

## Use of HAS-BLED to Assess Bleeding Risk in AF Patients

The acronym HAS-BLED represents each of the bleeding risk factors and assigns 1 point for the presence of each of the following: hypertension (uncontrolled systolic blood pressure >160 mm Hg), abnormal renal and/or liver function, previous stroke, bleeding history or predisposition, labile international normalized ratios, elderly, and concomitant drugs and/or alcohol excess.[15] The HAS-BLED scores range

**Table 4. Bleeding Risk Stratification Schemas**

| Authors | Bleeding Risk | | | Calculation of Bleeding Risk Score |
|---|---|---|---|---|
| | Low | Moderate | High | |
| Beyth et al,[28] 1998 | 0 | 1–2 | ≥3 | OBRI: age ≥65 y, GI bleed in last 2 wk, previous stroke, comorbidities (recent MI, Hct <30%, diabetes mellitus, creatinine >1.5 mL/L); 1 point for presence of each, 0 if absent |
| Kuijer et al,[27] 1999 | 0 | 1–3 | >3 | (1.6×age)+(1.3×sex)+(2.2×malignancy); 1 point for age ≥60 y, female, or malignancy, 0 if absent |
| Gage et al,[26] 2006 | 0–1 | 2–3 | ≥4 | $HEMORR_2HAGES$: liver/renal disease, alcohol abuse, malignancy, age >75 y, low platelet count/function, rebleeding risk, uncontrolled hypertension, anemia, genetic factors (eg, CYP2C9), risk of falls or stroke; 1 point for each, 2 points for previous bleed |
| Shireman et al,[25] 2006 | ≤1.07 | >1.07–<2.19 | ≥2.19 | (0.49×age >70 y)+(0.32×female)+(0.58×remote bleed)+(0.62×recent bleed)+(0.71×alcohol/drug abuse)+(0.27×diabetes mellitus)+(0.86×anemia)+(0.32×antiplatelet drug use); 1 point for presence of each, 0 if absent |
| Pisters et al,[15] 2010 | 0 | 1–2 | ≥3 | HAS-BLED: uncontrolled hypertension, abnormal renal/liver function (1 point each), stroke, bleeding history or predisposition, labile INR, elderly, concomitant drugs/alcohol excess (1 point each) |
| Fang et al,[24] 2011 | 0–3 | 4 | 5–10 | ATRIA: anemia (3 points), severe renal disease (eg, glomerular filtration rate ≤30 mL/min or dialysis dependent, 3 points), age >75 y (2 points), prior bleeding (1 point), and hypertension (1 point) |

ATRIA indicates Anticoagulation and Risk Factors in Atrial Fibrillation; INR, international normalized ratio; OBRI, Outpatient Bleeding Risk Index; GI, gastrointestinal; MI, myocardial infarction; and Hct, hematocrit.

from 0 to 9, with scores of ≥3 indicating high risk of bleeding, for which caution and regular review of the patient are recommended. In the original validation in the Euro Heart Survey,[15] the predictive accuracy of the HAS-BLED score was compared against another bleeding risk score, $HEMORR_2HAGES$,[26] and revealed similar C statistics of 0.72 and 0.66, respectively, for the overall validation cohort. In analyses among those patients receiving no antithrombotic therapy or antiplatelet therapy, HAS-BLED demonstrated better accuracy at predicting the risk of major bleeding (with C statistics of 0.85 and 0.91, respectively). The HAS-BLED score has also been validated in several different cohorts, including large real-world and clinical trial populations, as recently reviewed in a comprehensive European consensus document.[23] Overall, HAS-BLED offers better prediction of bleeding compared with many other bleeding risk scores,[29,30] although once again the predictive accuracy varies, depending on the cohort in which it is validated. In addition, the advantage of HAS-BLED over other bleeding risk scores is that it more user friendly and is made up of clinical information that is routinely available before therapy is initiated (with the exception of international normalized ratio values), thereby making it more clinically applicable.

HAS-BLED should not be used on its own to exclude patients from OAC therapy; it allows the clinician to identify bleeding risk factors and to correct those that are modifiable, ie, by controlling blood pressure, removing concomitant antiplatelet or nonsteroidal antiinflammatory drugs, and counseling the patient about reducing alcohol intake (if excessive). Thus, bleeding risk assessment with HAS-BLED should not be used as an excuse not to prescribe OAC but rather to highlight those patients in whom caution with such treatment and regular review is warranted.

## Patients' Values and Preferences for Treatment

It is also important to consider patients' preferences for antithrombotic therapy because many patients are often willing to accept a higher risk of bleeding to avoid a stroke. Education is essential because patients need to be fully informed of the risks and benefits of OAC therapy to enable them to make an informed decision about treatment and to be aware of the potential consequences of their decision.

## Net Clinical Benefit of OAC: Warfarin and Novel OAC Agents

When making treatment decisions about stroke thromboprophylaxis, you must balance the benefits of treatment (ie, stroke prevention) with minimizing the risk of serious bleeding complications (ie, intracranial hemorrhage) associated with such therapy in assessing the net clinical benefit.

A recent analysis was undertaken of the net clinical benefit (balancing ischemic stroke and intracranial hemorrhage) of vitamin K antagonist in a real-world nationwide Danish cohort of >130 000 people in whom stroke risk was assessed by both $CHADS_2$ and $CHA_2DS_2$-VASc and bleeding by HAS-BLED.[31] This analysis revealed that there was a positive net clinical benefit with vitamin K antagonist alone in patients with $CHADS_2$ ≥1 and a $CHA_2DS_2$-VASc score ≥2. The

net clinical benefit with a vitamin K antagonist was higher in patients with a high risk of bleeding (HAS-BLED score ≥3). There was a neutral net clinical benefit with $CHADS_2$ score of 0 and $CHA_2DS_2$-VASc score of 1. The only group in which vitamin K antagonist was associated a negative net clinical benefit was made up of patients with a $CHA_2DS_2$-VASc score of 0, a reflection of their truly low-risk status. Aspirin alone was not associated with a positive net clinical benefit at any risk strata; therefore, aspirin is not a good option if we seriously intend to prevent stroke in AF.[31]

Given the gradual availability of novel OAC drugs and in the absence of a head-to-head comparison of these drugs in clinical trials, a modeling analysis of the net clinical benefit (based on the risk of ischemic stroke and intracranial hemorrhage reported in these clinical trials) of dabigatran, rivaroxaban, and apixaban undertaken in the nationwide Danish cohort[32] may help to inform clinical decision making. In patients with a $CHADS_2$ score of 0 but with a high risk of bleeding, apixaban and dabigatran had a positive net clinical benefit. In patients with a $CHA_2DS_2$-VASc score of 1, apixaban and both doses of dabigatran (150 and 110 mg twice daily) had a positive net clinical benefit. All 3 novel OACs, dabigatran, rivaroxaban, and apixaban, appear to offer superior net clinical benefit over warfarin in patients with a $CHADS_2$ score ≥1 or $CHA_2DS_2$-VASc score ≥2, regardless of bleeding risk. When the risks of stroke and bleeding are both elevated, dabigatran, rivaroxaban, and apixaban appear to have a greater net clinical benefit than warfarin.[32]

## Conclusions

AF is a very common, often asymptomatic, condition that can present for the first time as a devastating stroke. The decisions about appropriate stroke thromboprophylaxis require individual assessment of stroke risk and risk of bleeding on such therapy. Use of risk schemas such as $CHA_2DS_2$-VASc and HAS-BLED can help to inform the choice of antithrombotic agent and the management strategy. Discussion of these risks with the patient is essential, and regular review of the risk profiles over the patient's lifetime/treatment course is essential to reduce the likelihood of adverse events.

These aspects were highlighted in a recent Consensus Conference organized by the Royal College of Physicians of Edinburgh on March 1 to 2, 2012. The key recommendations are summarized as follows[33]:

- Detection of AF must be improved; a national screening program should be introduced.
- Uptake of OAC must be increased, and methods of engaging patients in their AF management should be improved.
- Aspirin should not be used for stroke prevention in AF.
- In relation to rate and rhythm control for AF, relief of symptoms should be the goal of treatment.

The Royal College of Physicians of Edinburgh consensus statement[31] also highlighted that all patients with AF should have a formal stroke risk assessment with a scoring tool such as $CHA_2DS_2$-VASc. It also states that the use of the HAS-BLED score can help identify modifiable bleeding risks that need to be addressed but emphasizes that it should not be used on its own to exclude patients from OAC therapy.

## Case Disposition

The case study illustrates the implications of the choice of stroke risk stratification tool on the patient's treatment. Her HAS-BLED score is 1 (because of age of 65 years), indicating that her risk of bleeding on OAC is low. If this patient's stroke risk were assessed with the $CHADS_2$ score, she would score 0 and therefore be prescribed either aspirin or no antithrombotic therapy. In contrast, with the use of the $CHA_2DS_2$-VASc score, this patient would score 3 (female sex, age of 65 years, and previous myocardial infarction [vascular disease]; 1 point each), placing her at high risk of stroke and therefore making her a candidate for OAC. We used the latter scoring system and initiated OAC.

## Disclosures

Dr Lane has received research funding and/or honoraria for educational symposia from Boehringer Ingelheim, Bayer Healthcare, and Bristol Myers Squibb/Pfizer in relation to AF. Dr Lane is also a panelist on the Ninth Edition of the American College of Chest Physicians Guidelines on Antithrombotic Therapy. Dr Lip has served as a consultant for Bayer, Astellas, Merck, Sanofi, BMS/Pfizer, Daiichi-Sankyo, Biotronik, Portola, and Boehringer Ingelheim and has been on the speakers' bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, and Sanofi Aventis.

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