A Novel User-Friendly Score (HAS-BLED) To Assess 1-Year Risk of Major Bleeding in Patients With Atrial Fibrillation: The Euro Heart Survey

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Atrial fibrillation (AF) is associated with a well-known increase in ischemic stroke risk,\(^1\) which is further increased by individual conditions such as heart failure, hypertension, diabetes, and prior thromboembolism.\(^2\) Oral anticoagulation (OAC) dramatically reduces this risk\(^3\) and is therefore recommended in patients with AF at moderate-high risk of stroke and thromboembolism.\(^4\) The increasing incidence and prevalence of AF increases the likelihood of OAC use in the AF population, which is usually elderly, and comorbidities commonly coexist.\(^5\)\(^-\)\(^7\) Indeed, clinical decision making about whether OAC is justified based on stroke risk is supported by various practical stroke risk classification schema that incorporate known clinical risk factors.\(^8\)\(^-\)\(^9\)

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However, stroke risk is also closely related to bleeding risk,\(^6\) and OAC prescription needs to balance the benefit from stroke prevention against the risk of bleeding. Thus, there is often suboptimal
implementation of thromboprophylaxis among patients with AF which may be partly due to the lack of a validated bleeding risk-stratification schema that is user-friendly. This is further reflected by the absence of recommendations on bleeding risk assessment in current antithrombotic guidelines for AF management. The available schemas estimating the risk of bleeding associated with use of OAC either do not focus on patients with AF in particular, or incorporate routinely unavailable risk factors that also overlap significantly with stroke risk factors. Furthermore, all published schemas are based on historical cohorts of patients and consequently may not reflect advancements in medical care over time (for example, OAC monitoring) and treatment of underlying heart disease. Our aim was to develop a practical risk score to estimate the 1-year risk of major bleeding (intracranial, hospitalization, hemoglobin decrease > 2 g/L, and/or transfusion) in a contemporary, real-world cohort of patients with AF.

Materials and Methods

We used the large population database of the prospective Euro Heart Survey on AF, with data collected between 2003 and 2004. A detailed study outline of the Euro Heart Survey on AF at baseline and follow-up assessment has been previously described. In summary, 5,333 ambulatory and hospitalized patients with AF from 182 university, nonuniversity, and specialized hospitals among 35 member countries of the European Society of Cardiology were enrolled. Patients had to be ≥ 18 years of age and have an ECG or Holter proven diagnosis of AF during the qualifying admission or in the preceding year. A 1-year follow-up assessment was performed to determine survival and major adverse cardiovascular events, such as major bleeding. Medical records and/or medical information systems were used to populate the data set.

We defined major bleeding as any bleeding requiring hospitalization and/or causing a decrease in hemoglobin level of > 2 g/L and/or requiring blood transfusion that was not a hemorrhagic stroke. Hemorrhagic stroke was defined as a focal neurologic deficit of sudden onset, diagnosed by a neurologist, lasting > 24 h and caused by bleeding. Presence of chronic dialysis, renal transplantation, or serum creatinine ≥ 200 μmol/L was classified as abnormal kidney function. Abnormal liver function was defined as chronic hepatic disease (eg, cirrhosis) or biochemical evidence of significant hepatic derangement (eg, bilirubin > 2 upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase > 3 upper limit normal, and so forth). Finally, valvular heart disease was defined as the presence of any regurgitation or gradient over a valve with hemodynamic significance and/or related symptoms.

Statistical Analysis and Design of a New Bleeding Risk Score

Data analysis was performed with SPSS, version 16.0 (SPSS Inc., Chicago, IL). The presence of any differences between the groups with and without major bleeding during 1-year follow-up was tested by Fisher exact test for categorical variables and by independent samples t test for continuous variables.

All potential bleeding risk factors identified from the univariate analyses of the derivation cohort with a P value < .10 (age > 65 years, female sex, diabetes mellitus, heart failure, COPD, valvular heart disease, kidney failure, prior major bleeding episode, and clopidogrel use), were used in the multivariate logistic regression analyses along with more historical bleeding risk factors: OAC, alcohol use, and hypertension. We disregarded thyroid disease (P = .039) because of difficulties with interpretation (only n = 10 bleeding events), and this had not been identified as a bleeding risk in prior systematic reviews. Given the persistent nature of the evidence of OAC, hypertension, age > 65 years, renal failure, alcohol abuse, and prior major bleeding risk factors, these variables were kept in the model at all times. The other, less strongly linked variables were removed stepwise from the model when the P value was > .10. Variables with P < .05 in the final model were considered to be significant contributors and were checked for interaction effects, which did not exist.

In recognition of the limited number of major bleeds and relatively short follow-up period in the Euro Heart Survey on AF, we also added consistent risk factors for major bleeding (stroke, alcohol use, systolic BP > 160 mm Hg, and so forth) identified in recent systematic reviews to use the data from the derivation cohort to test a new bleeding risk score in a final statistical model, accepting the lack of statistical significance of some variables in our derivation cohort. For each of the variables in the final model the regression coefficient, net OR, and its 95% CI and P value are reported (Table 1). We then calculated the C statistic as a measure of the predictive accuracy of the model incorporating bleeding risk factors from the derivation cohort (that is, prior major bleeding, age > 65 years, clopidogrel use, and kidney failure), where, based on their respective multivariate regression coefficients, two points were awarded for prior major bleeding and one point for each of the other bleeding risk factors. In addition, we report the C statistics in a subgroup analysis of individuals discharged with OAC monotherapy, OAC combined with an antiplatelet drug, an antiplatelet drug alone, or no antithrombotic therapy. A new bleeding risk score (termed HAS-BLED) was calculated, incorporating risk factors from the derivation cohort as well as significant risk factors for major bleeding found in the literature from systematic reviews. HAS-BLED is an acronym for hypertensive (uncontrolled, > 160 mm Hg systolic), abnormal renal/liver function (one point for presence of renal or liver impairment, maximum two points), stroke (previous history, particularly lacunar), bleeding history or predisposition (anemia), labile international normalized ratio (INR) (ie, therapeutic time in range < 60%), elderly ( > 65 years), drugs/alcohol concomitantly (antiplatelet

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agents, nonsteroidal antiinflammatory drugs; one point for drugs plus one point for alcohol excess, maximum two points) as shown in Table 2.

In order to compare the predictive accuracy of our novel bleed risk score (HAS-BLED) with the previously proposed HEMORRHAGES (Hepatic or renal disease, Ethanol abuse, Malignancy, Older age [>75 years], Rebleeding, Reduced platelet count or function, Hypertension [uncontrolled], Anemia, Genetic factors, Excessive fall risk, and Stroke) scheme, patients were classified accordingly⁹; however, we considered “uncontrolled hypertension” to be >160 mm Hg systolic, a “history of malignancy” to be similar to “current malignancy,” and we classified ≥8 units alcoholic consumption per week as “ethanol abuse.” Relevant genetic and laboratory data (required for calculation of the HEMORRHAGES schema), apart from serum creatinine, were not available for the Euro Heart Survey on AF cohort.

### Table 2—Clinical Characteristics Composing the HAS-BLED Bleeding Risk Score

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical Characteristic</th>
<th>Points Awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function</td>
<td>1 or 2 (1 point each)</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years), Drugs/alcohol concomitantly; INR = international normalized ratio.

⁹See “Materials and Methods” for definitions of the clinical characteristics.

### Results

Of the 5,272 patients with AF in the Euro Heart Survey of AF who were discharged alive, 3,456 (66%) patients without mitral valve stenosis or valvular surgery had 1-year follow-up status regarding major bleeding. The overall mean (SD) age was 66.8 (12.8) years, and the majority were men (59%). Fifty-three (1.5%) patients experienced a major bleed during the first year, including nine (17%) cases of intracerebral hemorrhage. The baseline demographic and clinical characteristics of the 3,456 patients are presented in Table 3.

Of all discharged patients, 2,242 (44.8%) were on OAC (286 [12.8%] of whom also received aspirin and/or clopidogrel), 828 (24.0%) received antiplatelet therapy alone (aspirin and/or clopidogrel), and 352 (10.2%) received no antithrombotic therapy. The distribution of the risk factors for major bleeding within 1 year among the different antithrombotic treatment regimens in the derivation cohort is depicted.

### Table 3—Baseline Characteristics of Patients With Atrial Fibrillation From the Euro Heart Survey With a Known Follow-up Status Regarding Major Bleeding

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bleed (n = 53)</th>
<th>No Bleed (n = 3,910)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>73 (10)</td>
<td>66 (13)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age &gt;65 y</td>
<td>42 (79)</td>
<td>1,748 (51)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>28 (53)</td>
<td>1,329 (39)</td>
<td>.046</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>27 (5)</td>
<td>28 (8)</td>
<td>.298</td>
</tr>
<tr>
<td>Atrial fibrillation type</td>
<td>First detected</td>
<td>9 (17)</td>
<td>628 (19)</td>
</tr>
<tr>
<td></td>
<td>Paroxysmal</td>
<td>15 (28)</td>
<td>1,029 (31)</td>
</tr>
<tr>
<td></td>
<td>Persistent/permanent</td>
<td>29 (56)</td>
<td>1,688 (51)</td>
</tr>
<tr>
<td>Medical history</td>
<td>Current smoker</td>
<td>6 (11)</td>
<td>450 (13)</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
<td>39 (74)</td>
<td>2,228 (65)</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>12 (23)</td>
<td>610 (18)</td>
</tr>
<tr>
<td></td>
<td>Coronary artery disease</td>
<td>15 (29)</td>
<td>1,182 (35)</td>
</tr>
<tr>
<td></td>
<td>Heart failure</td>
<td>24 (45)</td>
<td>994 (24)</td>
</tr>
<tr>
<td></td>
<td>Valvular heart disease</td>
<td>18 (34)</td>
<td>607 (18)</td>
</tr>
<tr>
<td></td>
<td>COPD</td>
<td>12 (23)</td>
<td>427 (13)</td>
</tr>
<tr>
<td></td>
<td>Thyroid disease</td>
<td>10 (20)</td>
<td>326 (10)</td>
</tr>
<tr>
<td></td>
<td>Stroke/transient ischemic attack</td>
<td>6 (12)</td>
<td>355 (11)</td>
</tr>
<tr>
<td>CHADS₂ score, mean (SD)</td>
<td>2.07 (1.16)</td>
<td>1.60 (1.27)</td>
<td>.008</td>
</tr>
</tbody>
</table>

Values presented are No. (%) unless otherwise indicated. CHADS₂ = congestive heart failure, hypertension, age >75, diabetes mellitus, and previous stroke/transient ischemic attack (doubled).
The risk of major bleeding within 1 year in patients with AF in the Euro Heart Survey determined by the novel bleeding risk score, HAS-BLED, is shown in Table 5. The annual bleeding rate increased with the addition of each risk factor from the derivation cohort (Table 5).

The corresponding unadjusted bleeding rates in patients with OAC, antiplatelet therapy alone, or no antithrombotic treatment were 1.75, 0.97, and 1.42 bleeds per 100 patient-years, respectively. The predictive accuracy in the overall population using significant risk factors in the derivation cohort (C statistic 0.72) was consistent when applied in several subgroups, as shown in Table 6. Application of the new bleeding risk score (HAS-BLED) gave similar C statistics to that derived in the derivation cohort overall (0.72), or when patients were established on OAC at baseline (0.69), or when patients were on OAC plus antiplatelet therapy at baseline (0.78). HAS-BLED substantially improved the predictive accuracy of bleeding risk when patients with AF were receiving antiplatelet therapy alone or in those who were not on antithrombotic therapy at all (with C statistics of 0.91 and 0.85, respectively). The HEMOR-RHAGES bleeding scheme had a lower predictive accuracy compared with the new HAS-BLED score, overall or in relation to antithrombotic therapy use, except in the OAC plus antiplatelet therapy subgroup (Table 6).

Of all the 33 bleeding events in patients discharged with OAC because of a CHADS$_2$ (congestive heart failure, hypertension, age $\geq$ 75 years, diabetes mellitus, and previous stroke/transient ischemic attack [doubled]) score $\geq$ 1, four (12%) patients had a HAS-BLED-based bleeding risk that outweighed their individual stroke risk. Conversely, of all 1,580 patients discharged with OAC because of a CHADS$_2$ score $\geq$ 1 who did not suffer a major bleed within 1 year, only 34 (2.2%) had a HAS-BLED-based bleeding risk that outweighed their individual stroke risk. Of all 21 patients with a CHADS$_2$ score $\geq$ 1 discharged without OAC who suffered a stroke within 1 year of follow-up, only one had a HAS-BLED score outweighing the individual stroke risk. Of the patients with CHADS$_2$ score $\geq$ 1 who were discharged without OAC with a higher HAS-BLED bleeding risk score, all three patients suffered a major bleed.

**Discussion**

Using a derivation cohort based on the large, real-world population of the Euro Heart Survey on AF, we identified four independent risk factors of major bleeding within 1 year (prior major bleeding, age $\geq$ 65 years, clopidogrel use, and kidney failure). Incorporating these risk factors with other established risk factors from systematic reviews and multivariate analyses, we developed and tested a novel, user-friendly bleeding risk score, HAS-BLED, which demonstrated a good predictive accuracy in the overall Euro Heart survey cohort (C statistic 0.72) but performed particularly well in predicting bleeding risk where antiplatelet therapy was used alone (C statistic 0.91), or no antithrombotic therapy at all (C statistic 0.85). Assessment of both stroke and bleed risk using the CHADS$_2$ and HAS-BLED schemas, respectively, in the Euro Heart Survey on AF population would have resulted in withholding OAC therapy in 12% of the patients who suffered a major bleed within 1 year and the initiation of OAC in 95% of the patients at high risk for stroke who were discharged without OAC and had suffered a stroke within 1 year.

With the previously published HEMOR-RHAGES schema and others, the concept of a risk score for major bleeding in patients with AF is not new. However, our novel, proposed HAS-BLED score has several key advantages over the previously mentioned bleeding risk stratification method. First, the shorter acronym means that physicians have fewer risk factors to memorize when using the HAS-BLED score, thereby increasing the user-friendliness and subsequent clinical application. Furthermore, in contrast to certain risk factors incorporated into the HEMOR-RHAGES score that require laboratory parameters or even genetic testing, all risk factors of the HAS-BLED score are either readily available from the clinical medical history or routinely tested in (new) patients with AF. This characteristic strongly supports its use in all health-care settings and is another significant contributor to its superior user-friendliness. Because less does not necessarily mean more, it is important to note that the predictive accuracy of the HAS-BLED score is broadly similar when compared with the HEMOR-RHAGES model in the overall population (C statistic of 0.72 vs 0.66,

<table>
<thead>
<tr>
<th>Bleeding Risk Factor</th>
<th>Oral Anticoagulation (n = 2,115)</th>
<th>Aspirin/ Clopidogrel (n = 828)</th>
<th>Neither (n = 352)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP $&gt;160$ mm Hg</td>
<td>10.0</td>
<td>13.4</td>
<td>13.7</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>5.3</td>
<td>4.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.9</td>
<td>5.0</td>
<td>3.2</td>
</tr>
<tr>
<td>Prior major bleeding</td>
<td>1.7</td>
<td>1.6</td>
<td>3.2</td>
</tr>
<tr>
<td>Age $&gt;65$ y</td>
<td>53.3</td>
<td>52.8</td>
<td>42.6</td>
</tr>
<tr>
<td>Antiplatelet agent</td>
<td>12.1</td>
<td>100</td>
<td>0.0</td>
</tr>
<tr>
<td>Alcohol use$^a$</td>
<td>5.7</td>
<td>4.8</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Data shown as percentages.

$^a$ $\geq$ 8 U/wk.

Table 4—Clinical Risk Factors for Major Bleeding Within 1 Year in Patients With Atrial Fibrillation of the Euro Heart Survey According to Antithrombotic Treatment at Discharge

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of 0.85 vs 0.81, respectively), the HAS-BLED score is simpler. This score would be particularly useful in everyday clinical practice, when making decisions on whether OAC can be initiated in a patient newly diagnosed with AF who is not taking any antithrombotic therapy, or when antiplatelet therapy (or Nonsteroidal antiinflammatory drugs) use is being considered, for example, in the setting of coronary artery disease.

As mentioned previously, balancing the individual risk of bleeding and stroke is difficult but of the utmost importance to maximize appropriate antithrombotic therapy and minimize adverse events in patients with AF, resulting in a net clinical benefit for the treated patient. In daily clinical practice, the CHADS2 index is a widely used tool to stratify stroke risk in patients with AF. For now, the HEMOR2 RHAGES score is the only suitable counterpart available to assess the risk of bleeding in AF patients. Closer examination of the risk factors composing the CHADS2 and HEMOR2 RHAGES schemas reveals an extensive overlap between risk factors for bleeding and stroke, which has obvious drawbacks. Indeed, the patients at highest stroke and thromboembolic risk are paradoxically more likely to sustain bleeding complications. This may lead to confusion when trying to decide on the most appropriate antithrombotic regimen to balance the risks of bleeding against the risk of stroke, thereby limiting the applicability of such schemas.

The trade-off in terms of the benefits and risks of OAC using the CHADS2 index and HAS-BLED score demonstrates that in the vast majority of patients with AF who require OAC (CHADS2 index ≥ 2), the risk of bleeding outweighs the potential benefit of OAC if the HAS-BLED bleed score exceeds the individual CHADS2 index. In the case of a CHADS2 score of 1, the HAS-BLED score must exceed 2 for the potential harm caused by OAC to offset its beneficial effect.
on stroke risk reduction. Appropriate use of this practical rule in the Euro Heart Survey on AF population could have prevented more than one out of every 10 (4/33) of the major bleeds. However, 34/1,580 (2.2%) of the patients with a CHADS$_2$ score $\geq$ 1 discharged with OAC who did not suffer a major bleed within 1 year would have been denied OAC because of a HAS-BLED bleed risk outweighing their stroke risk.

The potential impact on current clinical practice of the novel HAS-BLED score is underlined by the recently published Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events-A (ACTIVE-A) trial. This large randomized clinical trial was designed to compare the preventive effect on all-cause vascular events of clopidogrel plus aspirin vs aspirin alone in patients with AF deemed unsuitable for OAC treatment. In half ($n = \sim 3,500$) of these patients with AF with a high stroke risk, the most common applied classification was “unsuitable for OAC,” which was solely based on physician clinical judgment, without the presence of any predefined risk factor of bleeding or other objective risk scoring. Perhaps this reflects physicians’ uncertainty about what to consider as true risk factors of bleeding and their fear of potential iatrogenic harm caused by OAC use.

Given the recent promising results of the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, patients assessed as being at higher bleeding risk using the novel HAS-BLED score could be prescribed the lower dose (110 mg bid) of the oral direct thrombin inhibitor, dabigatran, which demonstrated a significant reduction in major bleeding compared with warfarin, with a similar stroke risk reduction to warfarin, whereas those at lower bleeding risk could be prescribed dabigatran 150 mg bid, which offers superior efficacy but a similar major bleeding risk to warfarin. Further, the HAS-BLED score could also be used to identify patients who may benefit from a left atrial appendage occlusion device (ie, patients at high risk of ischemic stroke who have such an increased risk of bleeding that OAC is contraindicated). Thus, physicians initiating OAC (whether with the vitamin K antagonist or new oral anticoagulants, such as dabigatran) in a patient with AF could use the HAS-BLED score to assess the potential bleeding risk and feel more confident in prescribing OAC as appropriate or refer the patient for implantation of a left atrial appendage occlusion device. Indeed, bleeding risk scores should also be validated in dabigatran-treated patients, as well as those being considered for left atrial appendage occlusion devices.

Limitations

The HAS-BLED score needs to be validated in at least one other large contemporary cohort of patients with AF before it can be widely implemented into daily practice. Potential selection bias might have occurred because of 25% missing data regarding the occurrence of major bleeding during the follow-up period. Patients who were lost to follow-up were likely to have had more comorbidities and transferred to nursing homes or even have died, which might have led to underestimation of the overall bleeding rate. Also, we recognize that the limited number of major bleeds and the relatively short follow-up period make it possible that other important risk factors for bleeding were not identified. Indeed, bleeding may occur following changes to warfarin (eg, for surgery or interventions such as pacemaker implant) with institution of bridging therapy with low-molecular-heparin. We also did not consider thyroid disease in our model, as this had not been identified as a bleeding risk in prior systematic reviews; however, some pathophysiologic plausibility is possible, since hypothyroidism has been described to cause acquired von Willebrand disease associated with low factor VIII levels and platelet dysfunction. Of note, there is an improved predictive power of the HAS-BLED score over the HEMORRHAGES score in patients treated with antiplatelet therapy (or nonsteroidal antiinflammatory drugs) or no antithrombotic therapy at all (Table 6).

The risk of major bleeding (especially intracranial hemorrhage) is increased with advanced age. Of note, the risk of major hemorrhage can be similar among elderly patients receiving warfarin and aspirin. The relatively small numbers of bleeding events and the modest number of very elderly patients in our cohort makes it rather difficult to draw too many firm conclusions by introducing different weights to different age categories (eg, one point for age 65-74 years, two points for age 75-84 years, three points for age 85 years, and so forth), as well as introducing additional complexity to our simple HAS-BLED scoring system. Also, age is a continuous (rather than categorized) risk for bleeding (as well as stroke) and the biologic age of an elderly patient is probably more relevant to bleeding risk than the chronologic age. It must be stressed that in many instances, bleeding risk among the elderly is multifactorial and is often the result of associated comorbidities, high anticoagulation intensity, and labile INRs in this population. The HAS-BLED score already takes some of these aspects into account, allowing cumulative assessment of risk factors for bleeding. In the present analysis, the HAS-BLED score already outperforms the HEMORRHAGES bleeding scheme, which was an attempt by Gage et al to have a simple method of bleeding assessment. Future validation and refinement of HAS-BLED among a huge elderly AF population with prolonged follow-up may address the issue of age as a continuous variable for bleeding risk.
Finally, data about INR control are obviously not available when having to decide on starting OAC for the first time in a patient. When on OAC, the INR is often elevated at the time of admission for a bleeding event, but it is unknown which measure of INR control best predicts bleeding in such a manner that clinical action could prevent the bleeding. We did not include actual INR values during follow-up but acknowledge its importance as risk factor of bleeding. Of note, the current alternative (HEMOR$_3$RHADES model) was also developed without the availability of INR values.

**Conclusion**

We propose a novel bleeding risk score, HAS-BLED, that provides an easy, practical tool to assess the individual bleeding risk of patients with AF. The use of this simple score may potentially support clinical decision making regarding antithrombotic therapy for stroke prevention.

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**Author contributions:** Dr Pisters: contributed to statistical analyses, data interpretation, and drafting of the manuscript.

Dr Lane: contributed to drafting and revision of the manuscript.

Dr Nieuwlaat: contributed to statistical analyses, data interpretation, and drafting of the manuscript.

Dr de Vos: contributed to drafting and revision of the manuscript.

Dr Crijns: contributed to drafting and revision of the manuscript.

Dr Lip: contributed to study design and hypothesis, concept of the HAS-BLED score (the Birmingham Atrial Fibrillation Bleeding Risk schema), data interpretation, drafting of manuscript, and revisions.

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**References**


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