**Commentary**

**Considerations when choosing an appropriate bleeding risk assessment tool for patients with atrial fibrillation**

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Oral anticoagulation is integral to the management of patients with atrial fibrillation (AF) to reduce the risk of thromboembolism. Stroke risk should be assessed using the CHA2DS2-VASc score and men with a CHA2DS2-VASc score of ≥1 and women with CHA2DS2-VASc score ≥2 should be offered anticoagulation [1]. However, use of anticoagulation increases the risk of bleeding events and thus bleeding risk must be taken into account when initiating anticoagulation, especially since anticoagulation-related major bleeding in AF patients has been associated with a substantial increase in the risk of death, ischaemic stroke and myocardial infarction [2,3]. Intracranial haemorrhage, the most serious form of bleeding, was linked with a hazard ratio (HR) of 121.5 (95% confidence interval [CI], 91.3 - 161.8) for death and a HR of 22.0 (95% CI, 9.9 - 48.8) for stroke or myocardial infarction [2].

Several risk prediction models to determine risk of bleeding have been developed based on various clinical, biological and/or genetic markers [4–8]. The HAS-BLED score incorporates common bleeding risk factors for patients with AF [4] and is recommended by some guidelines for use in clinical practice [1,9].

However, bleeding risk scores have been used inappropriately by the ill-informed as an excuse to withhold anticoagulation. A high bleeding risk score (e.g., a HAS-BLED score of ≥3) is not a contraindication for oral anticoagulants, but instead should prompt responsible clinicians to undertake the necessary steps to reduce this risk and address modifiable risk factors such as uncontrolled hypertension, poor control of International Normalised Ratios (‘labile INRs’) if receiving a vitamin K antagonist, concomitant use of medications which increase the risk of bleeding including aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) and harmful alcohol consumption [10]. Other potentially modifiable risk factors for bleeding such as anaemia, impaired renal and/or hepatic function, and reduced platelet count or function should also be considered [10]. The HAS-BLED score is then used to flag up those ‘high risk’ patients for early review and follow-up (*e.g.* 4 weeks, rather than 4-6 months). It is vital that patients with AF who are at high-risk of bleeding are identified as early as possible, so potentially modifiable risk factors can be addressed and the patients can be appropriately monitored. The dynamic nature of risk also necessitates that regular assessments of bleeding (and stroke risk) are performed (**Figure 1**) as current evidence has demonstrated that changes in risk profiles are important predictors of adverse events in patients with AF [11–13].

Bleeding risk scores vary in their complexity and simplicity to implement in clinical practice [8]. Although the inclusion of additional factors may increase the accuracy of risk models, this is often at the expense of practicality and ease of calculation. Indeed, risk prediction, especially with incorporation of various biomarkers, can improve prediction (at least statistically) but at the cost of additional complexity, cost and reduced practicality [14]. There also exists a complex relationship between thrombosis and bleeding and several risk factors are shared (*e.g.* age, renal dysfunction and malignancy), which complicates clinical decisions. For the vast majority of patients with AF, the net clinical benefit of oral anticoagulation to reduce risk of stroke outweighs the risk of major bleeding, including among patients identified as being at high-risk of bleeding [15].

In the current issue of the *Journal of Thrombosis and Haemostasis*, Chang *et al.* [16] report the results from a network meta-analysis of 18 studies (n=321,888 patients) comparing the sensitivity and specificity of the HAS-BLED model and other risk assessment models for predicting major bleeding events in patients with AF. Overall, Chang *et al.* [16] show that the European score based only on modifiable bleeding risk factors, ABC and mOBRI models had high sensitivity but low specificity, while the ORBIT, ATRIA, Shireman and GARFIELD-AF models had high specificity, but low sensitivity. The network meta-analysis clearly demonstrates that the HAS-BLED model was the most balanced in terms of sensitivity and specificity, slightly surpassing the HEMORR2HAGES model.

These results provide an overview of the different bleeding risk models available and also quantitative evidence supporting the results of a previous systematic review which also concluded that the HAS-BLED provides the best prediction model for assessment of bleeding risk [17].

The study by Chang *et al.* [16] highlights some of the strengths and weaknesses of individual bleeding risk scores, particularly that those with a high sensitivity often had low specificity and *vice versa*. Although the HAS-BLED and HEMORR2HAGES models were balanced, both demonstrated only modest values of sensitivity and specificity. Modest values in both attributes may cause several limitations; indeed, scores with high sensitivity, but low specificity or scores with high specificity, but low sensitivity may be more useful in certain situations [18]. For instance, the ORBIT model had high specificity and would identify patients at high-risk of bleeding. Conversely, the mOBRI model had high sensitivity and could be used to confidently identify patients at low-risk of bleeding.

When employing the various bleeding risk models as screening tools, it is important to consider the characteristics of the cohort of interest, including the tendency for patients to have a high-risk of bleeding (Bayes’ theorem) [19]. As such, Chang *et al.* [16] appropriately suggest that among patients at high-risk of bleeding, a model with high sensitivity is desirable, while among patients at low-risk of bleeding, a model with high specificity is desirable.

However, sensitivity and specificity may be of little practical use for clinicians when considering the probability of bleeding events in individual patients. During such situations, the predictive probabilities (positive and negative predictive values [PPV; NPV]) of the various models are more important [18]. Thus, a model with high sensitivity or specificity may have little value if it has low PPV and NPV, such that clinicians are unable to produce reliable results from their assessments. To expand on this, a model with high specificity but a low NPV may incorrectly classify a significant proportion of patients as low-risk of bleeding when they should have been identified at high-risk instead (‘false negatives’). In practice, this misclassification could result in anticoagulated patients with AF not receiving the appropriate monitoring and a lack of attention on modifiable risk factors for bleeding.

Of note, the HAS-BLED score also draws attention to several potentially reversible risk factors (uncontrolled hypertension [H]; labile International Normalised Ratio [L]; concomitant use of NSAIDs or excess alcohol [D]) when compared to other models such as mOBRI, ATRIA, ABC and GARFIELD-AF, which mostly consist of non-modifiable risk factors.

No one model for assessing bleeding risk for patients with AF has both high sensitivity and high specificity and provides a ‘best fit’ for every clinical situation. The important thing is that a formal bleeding risk assessment is undertaken in all patients initiating OAC and that bleeding risk scores, such as HAS-BLED are memorable acronyms/tools to assist in identifying and addressing modifiable risk factors and identifying which patients will require closer/more frequent follow-up to reduce risk (Figure 1).

In summary, bleeding risk scores in patients with AF should not be used as an excuse to avoid initiation of oral anticoagulation. Furthermore, anticoagulants should not be avoided solely because the patient is at an increased risk of falls. Patients with AF identified as high-risk of bleeding should be adequately monitored and appropriate strategies should be implemented to reduce the patient’s risk of bleeding when commencing anticoagulation.

**Addendum**:

WYD and SLH wrote the first draft and all authors provided critical revision.

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**Figure 1.** Stroke and bleeding risk assessment in patients with atrial fibrillation