ASSESSING RISK OF BLEEDING IN PATIENTS WITH ATRIAL FIBRILLATION

Multiple randomized trials have shown oral vitamin K antagonists to be highly effective in reducing stroke risk for patients with nonvalvular atrial fibrillation (AF).[1] The major risk of oral anticoagulants is bleeding. Vitamin K antagonists require regular monitoring of the international normalized ratio (INR), and poor compliance with monitoring or difficulty in maintaining a therapeutic INR has been cited as an additional risk factor for bleeding.[2] Recently, new-generation oral anticoagulants have been introduced for stroke prevention in nonvalvular AF. These drugs have the advantage of fixed dosing with no requirement for continued monitoring. They have been found to be noninferior to vitamin K antagonists for prevention of embolic events. They also have been shown to have relatively similar risks of bleeding.[3-5] Some analyses, however, have suggested that fixed dose oral anticoagulation may be superior in efficacy when compared to patients who have difficulty keeping the INR in the therapeutic range.[6]

Because of the perception of bleeding risk, patients may not be treated with oral anticoagulants or treated with platelet inhibiting agents as an alternative therapy despite conclusive evidence that oral anticoagulation is superior to antiplatelet agents alone for prevention of stroke in nonvalvular AF. The table below shows aggregate bleeding risks (defined as major extracranial nonfatal bleeds) for various therapies derived from large trials or meta-analyses.

TABLE 1. RISK OF MAJOR BLEEDING IN RANDOMIZED TRIALS/YEAR

Treatment Trial	No Therapy	Aspirin	Aspirin and Clopidogrel	Warfarin	New Oral Anticoagulants
6 RCT*[1]	0.5%	—		1.6%	—
60 RCT*[1]	0.7%	1.1%			—
11 RCT*[1]	—	1.3%		2.0%	—
Active-W[7]			2.4%	2.2%	
Active-A[8]		1.3%	2.0%		
AVERROES[3] (apixaban)	—	1.2%	—	—	1.4%
Combined SPORTIF III-IV[9] (ximelagatran)				2.9%	2.5%
RELY (110/150)[4] (dabigatran)				3.4%	2.7/3.1%
ROCKET-AF[5] (rivaroxaban)				3.4%	3.6%

**Meta-analysis performed comparing the different therapies listed.*

While global rates of bleeding risk are helpful, it is difficult to apply these values to individual patients. Just as the $CHADS_2$ and the CHA_2DS_2-VASc scoring systems have shown marked variation in risk of stroke, attempts have been made to establish point score systems for risk of bleeding. Multiple systems have been proposed and evaluated. The HAS-BLED score has emerged as the most user-friendly and rigorously tested point score system assessing bleeding risk.[10] The HAS-BLED scoring system is displayed in Table 2.[11]

TABLE 2. HAS-BLED SCORE

Letter	Clinical Issue	Points	Comment
H	Hypertension	1	Systolic pressure >160 mmHg
A	Abnormal renal or hepatic function	1 or 2	Renal: dialysis, chronic renal failure, GFR <50 hepatic: cirrhosis, hepatitis, bilirubin >2x upper normal, enzymes >3x upper normal
S	Stroke	1	
B	Bleeding	1	Previous major bleeding episode or predisposition to bleeding
L	Labile INR	1	High or unstable INR; INR in therapeutic range <60% of time
E	Elderly	1	>65 years old
D	Drugs	1 or 2	Concomitant use of antiplatelet drugs or NSAIDS; prior hospitalization for alcohol related disease or known heavy consumption

GFR=glomerular filtration rate. NSAIDs=non-steroidal anti-inflammatory drugs.

The performance of the HAS-BLED scoring system is demonstrated in Table 3. The original dataset used to derive the score is in the first column.[11] Subsequently, the scoring system has been tested in multiple additional cohorts of patients, three of which are shown in Table 3. All of the datasets show relatively similar increment in annual risk of bleeding related to this patient score.

TABLE 3. BLEEDING RISK SCORES AND BLEEDING RISK/YEAR

Score	Pisters, et al[11]	Gallego, et al[12]	Friberg, et al*[13]	Lip, et al[14]
0	1.1%	0	0	1.2%
1	1.0%	1.2%	0.7%	2.8%
2	1.9%	2.2%	1.9%	3.6%
3	3.7%	5.9%	2.4%	6.0%
4	8.7%	7.0%	3.4%	9.5%
≥5	12.5%	19.4%	5.7-15.5%	7.4%

**Oral anticoagulants only.*

Application of the HAS-BLED score should be considered an approximation. The clinical items that comprise each category of HAS-BLED are relative and subject to considerable interpretation by the clinician. Rather than being a scoring system that denies patients anticoagulation, the HAS-BLED score should be used as a relative indicator to help assess ongoing bleeding risk. The score may also point out factors that could be clinically adjusted in patients that might lower their annual bleeding risk, such as reassessment of the need for certain therapies or the intensity of treatment of blood pressure. Since the $CHADS_2$ and CHA_2DS_2-VASc scores frequently track in a parallel fashion with HAS-BLED, many patients with significant bleeding risk such as a HAS-BLED score >3 may still derive considerable benefit from anticoagulation because those same individuals might have a large stroke risk.[15]

Clinical Vignettes

1. A 60-year-old man with a known history of cirrhosis, a prior GI bleed of 6 units a year ago, and ongoing significant ethanol intake presents to the emergency department with AF. He is normotensive and has no known cardiac disease. Echocardiography shows a structurally normal heart. This patient has a HAS-BLED score of 3 and a $CHADS_2$ score of 0. His bleeding risk would be at least 3.7% per year, and his stroke risk should be very, very low. Therefore, this individual would not benefit from anticoagulation and would not benefit from aspirin.

2. A 70-year-old woman has a history of heart failure, dilated cardiomyopathy, and reduced renal function with an estimated GFR of 30. She is discovered to have AF on a routine clinic visit; the AF is asymptomatic. The patient has a CHA_2DS_2-VASc score of 3 and a HAS-BLED score of 2. The patient has a relatively low bleeding risk and a higher stroke risk, and thus would benefit from oral anticoagulation.

3. An 82-year-old woman with diabetes, claudication, and HTN presents with new-onset AF. Both CHADS scoring systems would estimate her stroke risk at about 4-4.5% per year. Despite the fact she is 82 years old, her HAS-BLED score is only 2 and thus her bleeding risk is approximately 2% per year. She would benefit from oral anticoagulation.

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