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North American Thrombosis Forum, AF Action Initiative Consensus Document

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ABSTRACT

The North American Thrombosis Forum Atrial Fibrillation Action Initiative consensus document is a comprehensive yet practical briefing document focusing on stroke and bleeding risk assessment in patients with atrial fibrillation, as well as recommendations regarding anticoagulation options and management. Despite the breadth of clinical trial data and guideline recommendation updates, many clinicians continue to struggle to synthesize the disparate information available. This problem slows the uptake and utilization of updated risk prediction tools and adoption of new oral anticoagulants. This document serves as a practical and educational reference for the entire medical community involved in the care of patients with atrial fibrillation.
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KEYWORDS: Anticoagulants; Antithrombotic management; Atrial fibrillation; Bleeding risk; Stroke

STROKE RISK STRATIFICATION

Atrial fibrillation (AF), the most frequently encountered sustained cardiac arrhythmia, is a major risk factor for ischemic stroke.[1,2] On average, patients with AF have a fivefold higher risk for stroke than the general population.[3] However, an individual patient's risk of stroke

The North American Thrombosis Forum is a nonprofit organization focused on unmet needs and issues related to thrombosis and cardiovascular diseases such as atrial fibrillation, stroke, deep vein thrombosis, pulmonary embolism, myocardial infarction, and peripheral arterial occlusive disease. Learn more at: www.NATFonline.org. Although there are several alternative acronyms for novel oral anticoagulants (or non-vitamin K antagonist [VKA] oral anticoagulants) that have emerged, we have continued to use the traditional term "NOAC" throughout this document when referring to the Factor IIa (dabigatran) and Factor Xa (rivaroxaban, apixaban, and edoxaban) inhibitors to avoid the confusion that could result from acronym change and to facilitate the consistency of results when conducting literature or general Web searches.

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varies depending on the presence or absence of various risk factors.

Stroke risk stratification scores rely on a combination of demographic and clinical characteristics. The most well-known and validated stroke-risk stratification score is the $CHADS_2$ score (Table 1).[4] $CHADS_2$ scores have been broadly categorized as low (0), intermediate (1), and high (2-6) risk of stroke.[5] In older guidelines, anticoagulant therapy was recommended for high-risk patients, whereas an anticoagulant or aspirin was recommended for moderate-risk patients, and aspirin alone for low-risk patients.[1,4,6-8]

However, the traditional stroke risk-stratification schemes, including the $CHADS_2$ risk score, are limited by not sufficiently identifying truly "low-risk" patients by excluding other known stroke risk factors such as vascular disease (myocardial infarction and peripheral vascular disease) and female sex,[5] as well as consideration of the increased stroke risk that exists in patients younger than 75 years of age. Such exclusions lead to underestimation of stroke risk and result in undertreatment with oral anticoagulants for stroke prevention.

The more recently developed and validated CHA_2DS_2-VASc risk-stratification score[9-14] (Table 2) is a modification and expansion of the $CHADS_2$ scheme that incorporates additional stroke risk factors.[5] It offers the main advantage of better identifying "truly low-risk" individuals that likely do not benefit from anticoagulation. The annual rate of thromboembolic events associated with CHA_2DS_2-VASc = 0 was 0%, compared with 1.40% with $CHADS_2 = 0$ in the same patients. In the updated guidelines, anticoagulation should be considered for AF patients with $\geq$1 stroke risk factors or a CHA_2DS_2-VASc $\geq$1 (Table 3).[4,5,15,16]

CLINICAL SIGNIFICANCE

- The North American Thrombosis Forum Atrial Fibrillation Action Initiative consensus document is a comprehensive yet practical briefing document that provides a concise review of important clinical research and provides expert consensus recommendations regarding risk assessment and anticoagulation management.
- The document was developed to serve as a reference for both the medical community and patients.
- The document covers many management issues routinely encountered in clinical practice but not covered in conventional guideline recommendations.

BLEEDING RISK STRATIFICATION

Anticoagulants reduce the risk of AF-related thromboembolism, but also increase the risk of bleeding. Scoring systems that use clinical characteristics to estimate a patient's annual risk for major bleeding can help clinicians who wish to compare the risks and benefits of anticoagulation. Several such scoring systems[17-21] have been derived and validated for patients with AF who are taking warfarin (Table 4), although all have only modest ability to predict bleeding.

The quantitative approximation of bleeding risk provided by these models may have less importance than a familiarity with the individual risk factors themselves. For example, an awareness that renal disease has repeatedly emerged as an independent risk factor for warfarin-associated major bleeding should prompt increased attention to the net clinical benefit of anticoagulation for a patient with AF, especially if the risk of ischemic stroke is low. More importantly, the knowledge that poorly controlled hypertension, concomitant antiplatelet therapy, and alcohol abuse each independently increases bleeding risk provides the potential opportunity to increase the safety of anticoagulation when one or more of these factors can be modified.

In practice, many AF patients with a high risk of ischemic stroke also have a high risk of bleeding, as the same risk factors predict both outcomes.[22] Providers and patients who use risk scores such as $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; Table 5) should be aware that the severity of the clinical outcomes they predict can vary significantly (Table 6).[23] For example, a stroke can be relatively minor (eg, transient or insignificant neurologic deficit) or result in neurologic devastation (a large cerebral infarct with dense, permanent hemiparesis). Similarly, a major bleed can range from a slow diverticular leak to a fatal intracranial hemorrhage. Clinicians should also be cautioned that the currently available bleeding risk calculators were developed for patients on warfarin and not novel oral anticoagulants (NOACs). Further research will be needed to determine how existing bleeding risk scoring systems will require modification if used to weigh the hazards of prescribing an oral direct factor Xa or thrombin inhibitor.

In summary, the vast majority of AF patients encountered in clinical practice have a net clinical benefit from anticoagulation as their risk of ischemic stroke without anticoagulation far outweighs their risk of serious bleeding if prescribed an anticoagulant. Bleeding risk scores should not be used to justify withholding anticoagulation if the calculated score is above some threshold, but rather to help clinicians identify modifiable factors (such as unnecessary concomitant antiplatelet medication use or poorly controlled hypertension) that, if addressed, may reduce the risk of anticoagulant-associated major bleeding.

THE FUTURE OF RISK STRATIFICATION—BIOMARKERS AND GENETICS

Development of AF

AF frequently goes clinically unrecognized and undiagnosed,[24,25] and may first present as a stroke.[26] Subclinical AF