Antithrombotic and Anticoagulant Therapy for Atrial Fibrillation

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KEYWORDS

• Atrial fibrillation • Stroke risk • Bleeding risk • Antithrombotic prophylaxis • Oral anticoagulants • Antiplatelet drugs

KEY POINTS

- Prophylaxis of stroke and other thromboembolic events is central to the management of patients with atrial fibrillation (AF).
- All patients with AF, but with low risk of stroke (nonvalvular AF and CHA_2DS_2-VASc score = 0 in males or 1 in females), require treatment with oral anticoagulants (OACs) unless they are contraindicated.
- Vitamin K antagonists (VKAs) and non-VKA OACs (eg, dabigatran, rivaroxaban, apixaban) can be administered depending on the clinical situation.
- Antiplatelet drugs, either alone or in combination, are inferior to OACs for antithrombotic prophylaxis but have to be used in combination with OACs in AF patients undergoing percutaneous intervention with stent implantation.
- In high-risk patients with contraindications for anticoagulation, left atrial appendage exclusion is an alternative option.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia associated with high morbidity and mortality. The upward trend for AF prevalence translates into approximately 3% of adults being affected with arrhythmia in the more recent report.[1,2]

AF confers a 5-fold elevated risk of stroke, characterized by prolonged hospitalizations, greater disability, and higher mortality when associated with arrhythmia, in comparison with patients without AF.[3] In real life, involvement of AF in stroke development seems to be even more profound; a substantial proportion of so-called cryptogenic stroke AF has been detected via prolonged electrocardiogram monitoring, as AF per se is often asymptomatic.[4]

Oral anticoagulation (OAC) is the recommended effective option for the prevention of stroke and other thromboembolic events in AF, with either dose-adjusted vitamin K antagonists (VKAs) (eg, warfarin) or non-VKA anticoagulants (eg, dabigatran, apixaban, rivaroxaban, or edoxaban).[5,6] Antithrombotic prophylaxis with adherence to guidelines has improved significantly during the last decade, but the rate of antiplatelet drug

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administration instead of OAC remains significant, especially among the elderly and those at high risk of bleeding. In the EURObservational Research Programme Atrial Fibrillation General Pilot Survey (EORP-AF), for example, 95.6% of patients among those with the CHA_2DS_2-VASc score of 1 or higher, that is, with indications for OAC, received antithrombotic prophylaxis, with 80.5% of these taking OAC.[7] Another unfavorable trend found in the EORP-AF study was common administration of a combination of OAC with antiplatelet drugs in stable coronary artery disease (CAD).[7]

This article provides an overview of current evidence for antithrombotic therapy in patients with AF.

ASSESSMENT OF STROKE AND BLEEDING RISK

The risk for stroke is not homogeneous in AF patients. Thus, the decision to initiate OAC therapy has to be justified by the patient's individual risk assessment, and the net clinical benefit balancing stroke reduction against serious bleeding. A variety of risk factors for stroke development has been established, which subsequently formed the basis for various risk-stratification schemes for stroke.[8,9]

The CHA_2DS_2-VASc score[10] (see **Table 1** for expansion of the acronym) is recommended by the 2012 European Society of Cardiology and 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines for the management of AF as the only risk-assessment tool for stroke in patients with nonvalvular AF.[5,6]

The annual rate of thromboembolic events (including ischemic stroke, pulmonary embolism, and peripheral artery embolism) increases gradually with increasing CHA_2DS_2-VASc score, ranging from 0.78 (95% confidence interval [CI] 0.58–1.04) per 100 person-years with CHA_2DS_2-VASc = 0, rising to 23.64 (95% CI 10.62–52.61) with CHA_2DS_2-VASc = 9.[11]

The major advantage of the CHA_2DS_2-VASc score in comparison with other risk-stratification schemes for stroke, including the older $CHADS_2$ score (heart failure, hypertension, age $\geq$75 years, diabetes, and stroke/transient ischemic attack)[12] is its ability to reliably distinguish the group of patients with a low risk of stroke, that is, a CHA_2DS_2-VASc score of 0 for males or 1 for females, which has been validated in several large real-world AF cohorts.[13–15] For example, in a retrospective analysis performed in the Danish nationwide cohort study involving 19,444 patients with $CHADS_2$

Table 1
Risk stratification for stroke and bleeding using the CHA_2DS_2-VASc and HAS-BLED scores

CHA_2DS_2-VASc	Score	HAS-BLED	Score
Congestive heart failure/LV dysfunction	1	Hypertension (systolic blood pressure >160 mm Hg)	1
Hypertension	1	Abnormal renal or liver function	1 or 2
Age $\geq$75 y	2	Stroke	1
Diabetes mellitus	1	Bleeding tendency or predisposition	1
Stroke/TIA/TE	2	Labile INR (if on warfarin)	1
Vascular disease (prior MI, PAD, or aortic plaque)	1	Age (eg, >65 y, frail condition)	1
Age 65–74 y	1	Drugs (eg, concomitant antiplatelet or NSAIDs)	1 or 2
Sex category (ie, female gender)	1	or alcohol excess/abuse	
Maximum score	9		9

CHA_2DS_2-VASc: Heart failure (moderate to severe left ventricular systolic dysfunction referring to left ventricular ejection fraction $\leq$40% or recent decompensated heart failure requiring hospitalization), hypertension, age $\geq$75 years, diabetes, stroke/transient ischemic attack, vascular disease (specifically myocardial infarction, complex aortic plaque, and peripheral artery disease), age 65–74 years, female sex.

HAS-BLED: Uncontrolled hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (eg, age >65 years, frail condition), drugs (eg, antiplatelets, nonsteroidal anti-inflammatory drugs)/excessive alcohol.

Abbreviations: INR, international normalized ratio; LV, left ventricular; MI, myocardial infarction; NSAIDs, nonsteroidal anti-inflammatory drugs; PAD, peripheral artery disease; TIA/TE, transient ischemic attack/thromboembolism.

Data from Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest 2010;137(2):263–72; and Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010;138(5):1093–100.