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Atrial Fibrillation:

A Common Cause of Stroke

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Abstract

Atrial fibrillation is the culprit causal mechanism of twenty percent of acute ischemic strokes. As the population of Delaware ages, atrial fibrillation is a growing cause of stroke. Thus, the detection of atrial fibrillation and treatment of this cardioembolic risk factor of stroke is paramount.

Atrial Fibrillation Definitions

Atrial fibrillation (AF) is a type of cardiac arrhythmia characterized by irregular and often rapid electrical activity in the atria. During AF, the atria quiver instead of contracting normally, which can lead to an irregular heart rate and inefficient blood flow. AF can be classified into four types, by duration and if it is recurrent or sustained[1]:

1. Paroxysmal AF: AF that comes and goes on its own, typically lasting less than 7 days.
2. Persistent AF: AF that continues for longer than 7 days, or requires medical intervention to terminate.
3. Long-standing persistent AF: AF that lasts for more than 12 months.
4. Permanent AF: AF that is present and accepted as a permanent condition, and efforts to restore normal rhythm have been discontinued.[2]

AF can occur in individuals with underlying heart disease, such as hypertension, coronary artery disease, or heart failure, or it can occur in individuals without any known underlying heart disease. AF can be asymptomatic or may cause symptoms such as palpitations, shortness of breath, chest discomfort, and fatigue.[3]

Atrial Fibrillation Epidemiology

Atrial fibrillation (AF) is the most common arrhythmia in the United States, affecting approximately 2.7 million Americans. The prevalence of AF increases with age, with 5% of individuals over the age of 65 and 10% of those over the age of 80 having this condition.[4]

The incidence of AF is also increasing, with an estimated 160,000 new cases diagnosed each year. This increase is likely due to the aging population and the increasing prevalence of risk factors such as hypertension, obesity, and diabetes.[5] AF is more common in men than women, and in individuals of European descent compared to other racial and ethnic groups. However, it is important to note that AF can occur in anyone, regardless of age, gender, or ethnicity.[6]

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AF is associated with an increased risk of stroke, heart failure, and mortality. The burden of AF on the healthcare system is significant, with estimated costs of over $26 billion annually in United States.[1] AF contributes to more than 20% of acute ischemic strokes.[7]

Evaluation and Detection of Atrial Fibrillation

For patients with acute ischemic stroke, evaluation for occult AF is important. This should include electrocardiographic monitoring in the hospital for at least 24 hours.[8] For patients with a cryptogenic stroke who do not have a contraindication to anticoagulation, further testing with outpatient remote monitoring should be considered to evaluate for occult AF. Remote monitoring options include outpatient telemetry or an implantable cardiac monitor.

A 2016 randomized controlled trial showed AF in 30% of 221 patients with implantable cardiac monitors and in 3% of 220 control patients after 36 months of follow-up (hazard ratio 8.8; 95% CI = 3.5-22.2; P <0.0001).[9] It is unknown whether this monitoring with subsequent initiation of oral anticoagulants in affected patients will lower the rate of subsequent stroke, but it is now routine practice to offer prolonged cardiac monitoring for patients with embolic stroke of unknown source (ESUS type stroke).[10]

The American Heart Association/American Stroke Association (AHA/ASA) guidelines for stroke prevention in patients with previous stroke do not recommend an echocardiogram for all patients. However, they do advise that an echocardiogram be obtained for patients with cryptogenic stroke of unknown source to evaluate for structural heart pathology.[10] While transthoracic echocardiography (TTE) alone may not definitively predict the occurrence of AF, certain echocardiographic features have been associated with an increased risk of AF. These features include left atrial enlargement, left ventricular dysfunction, increased left ventricular mass, valvular heart disease, diastolic dysfunction, and left atrial appendage dysfunction.[11]

Treatment Options for Atrial Fibrillation

After the diagnosis of AF is made, it is important to decide who to treat with anti-coagulants. The CHA_2DS_2-VASc score is used to calculate the risk of ischemic stroke in patients with AF (Table 1).[12] For patients with nonvalvular AF, a CHA_2DS_2-VASc score of 2 or greater, and an acceptably low risk of bleeding, the 2019 AHA/ACC/Hearth Rhythm Society (HRS) guidelines for AF management suggest that the use of direct-acting oral anticoagulants (DOACs)-is preferable (Table 2).[13] For stroke prevention in these patients, recommended DOACs include apixaban (Eliquis, 5 mg 2 times/day), dabigatran (Pradaxa, 150 mg 2 times/day), and rivaroxaban (Xarelto, 20 mg once daily).[14]

Table 1. CHA_2DS_2-VASc Score to Estimate Stroke Risk in Patients With Atrial Fibrillation[12]

Risk Factor (score if yes)	**Number of Points**
Congestive heart failure history	1
Hypertension history	1
Age ≥75 years	2
Diabetes history	1
Stroke/TIA/thromboembolism history	2
Vascular disease history (prior MI, PAD)	1
Age 65-74 years	1

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Sex category - female	1
Age <65 years	0

CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or TIA or thromboembolism (doubled), vascular disease, age 65 to 74 years, sex category; MI = myocardial infarction; PAD = peripheral artery disease; TIA = transient ischemic attack.

Table 2. CHA_2DS_2-VASc Score Interpretation

Score	Risk of Ischemic Stroke (Event/Hundred Years at Risk)[a]
0	0.2
1	0.6
2	2.2
3	3.2
4	4.8
5	7.2
6	9.7
7	11.2
8	10.8[a]
9	12.2

[a] Data from the Friberg validation study, but in general would assume the higher the score, the higher the risk of ischemic stroke. CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or TIA or thromboembolism (doubled), vascular disease, age 65 to 74 years, sex category.

The criteria for modified dosages vary by drug. A reduced dosage of apixaban (2.5 mg 2 times/day) is recommended if two of three criteria are met: creatinine level of 1.5 mg/dL or greater, age 80 years or older, and body weight of 60 kg/132.3 lb or less. A reduced dosage of dabigatran (75 mg 2 times/day) is recommended for patients with a creatinine clearance of 15 to 30 mL/minute. A reduced dosage of rivaroxaban (15 mg once daily) is recommended for patients with a creatinine clearance of 50 mL/min or less.

Shared decision-making is indicated when prescribing these drugs, with patient preference, cost, and adherence being considerations.[13,14] Patients taking warfarin require regular monitoring to achieve and maintain a therapeutic INR. Warfarin is associated with substantial drug-drug interactions but its effects can be rapidly reversed. The DOACs have simpler dosing than warfarin.[15] Dabigatran, rivaroxaban, and apixaban appear to have similar effectiveness, although apixaban may be associated with lower bleeding risk and rivaroxaban may be associated with higher bleeding risk. Drugs to reverse the effects of DOACs now are available for emergency use.[15]

For patients with AF who need anticoagulation and who are also on hemodialysis, apixaban would be the novel oral anticoagulant of choice. The recommended dosage is 5 mg 2 times/day, with a dosage reduction to 2.5 mg 2 times/day for patients 80 years and older and with a body weight of 60 kg/132.28 lb or less.[3] Controversy exists as to whether any anticoagulant should be used in patients receiving dialysis given other risks of bleeding. Shared decision-making should

be used in prescribing these drugs.[13] The AHA/ACC/HRS guidelines suggest that warfarin or apixaban can be used in patients with end-stage renal disease.

The HAS-BLED (hypertension, abnormal liver/renal function, stroke, bleeding tendency/predisposition, labile INR, elderly [older than 65 years], drug/alcohol concomitantly) score can be used to calculate the risk of rebleeding in patients with a history of bleeding (Table 3 and Table 4).[16] It has been validated in patients taking warfarin but has not been studied in patients taking DOACs. If the annual risk of bleeding is higher than the annual risk of ischemic stroke, alternative stroke prophylaxis should be discussed with the patient and considered.[13]

Table 3, HAS-BLED Score to Estimate Bleeding Risk in Anticoagulated Patients With Atrial Fibrillation[16]

Risk Factor	Number of Points
Hypertension (uncontrolled, >160 mm Hg systolic)	1
Renal disease (Cr level >2.26 mg/dL, dialysis or transplant)	1
Liver disease (cirrhosis or bilirubin >2x ULN with AST/ALT/AP >3x ULN)	1
Stroke history	1
Prior major bleeding or predisposition to bleeding	1
Labile INR (unstable INR, time in therapeutic range <60%)	1
Elderly (age >65 years)	1
Drugs (predisposing to bleeding [aspirin, clopidogrel, NSAIDS])	1
Alcohol (≥8 drinks/week)	1

ALT = alanine aminotransferase; AP = alkaline phosphatase; AST = aspartate aminotransferase; Cr = creatinine; HAS-BLED = hypertension, abnormal liver/renal function, stroke, bleeding tendency/predisposition, labile INR, elderly (>65 years), drugs/alcohol concomitantly; INR = international normalized ratio; NSAIDs = nonsteroidal anti-inflammatory drugs; ULN = upper limits of normal.

Table 4. HAS-BLED Score Interpretation[17,18]

Score	Annual Risk of Major Bleeding (%)	Recommendation
0	0.9	Anticoagulation can be considered
1	3.4	
2	4.1	
3	5.8	More frequent monitoring and review of risk factors. Alternative to anticoagulation can be considered
4	8.9	
5	9.1	
>5	>10[a]	

[a]Data are limited, but a score >5 is thought to be associated with a high risk of bleeding.

Patients with AF who cannot undergo anticoagulation may be considered for placement of a left atrial appendage device, closure device, or surgical ligation of the left atrial appendage.[13,14] Use of a closure device has been found to be noninferior compared with a DOAC in preventing a

composite of stroke, transient ischemic attack (TIA), embolism, mortality, and bleeding in patients with AF.[19]

For patients who recently had stroke due to AF, the question when to re-initiate anti-coagulation often occurs. One recent large observational trial, the ELAN study, looked at this question.[20] Small stroke was defined as <1.5 cm size stroke. Moderate size stroke was one superficial branch occlusion. Large stroke was defined as involving one branch or more, or a >1.5cm infarct in the brainstem. The early group started anticoagulation in 48 hours for small/moderate strokes and on day 6-7 for large strokes. The late group had initiation of a DOAC in participants with a minor stroke on day 3 or 4 after stroke onset, in moderate strokes on day 6-7, and in participants with a major stroke on day 12-14. This study suggests that early re-initiation of anticoagulation is safe and better at preventing recurrent ischemic stroke (1.4% vs 2.5% in the late initiation group), without significant added burden of hemorrhage (0.2% in both groups).

In summary, recognition of AF and appropriate treatment of this risk factor is important in the prevention of acute ischemic stroke in the aging population.

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