Contemporary management of atrial fibrillation

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Abstract:

Nurse practitioners (NPs) frequently treat adults with atrial fibrillation. With new oral antithrombotic agents available, NPs need to be knowledgeable of treatment options to prevent stroke and systemic emboli. This article reviews the latest American College of Cardiology Foundation/American Heart Association guideline on the management of atrial fibrillation. Emphasis is placed on the changing landscape of pharmacological agents. Use of guideline-directed medical therapy will ultimately improve patients' quality of life and prevent stroke and premature death.

Keywords: anticoagulation | atrial fibrillation | clinical guidelines | nurse practitioner | stroke prevention

Article:

Atrial fibrillation (AF), the most common, sustained cardiac dysrhythmia in adults, is a condition that nurse practitioners (NPs) frequently encounter in clinical practice. Estimates of AF prevalence in the United States ranged from 2.7 million to 6.1 million individuals in 2010 and is predicted to double by 2050.[1] Furthermore, the Framingham Heart Study calculated that the lifetime risk for a 40-year-old man to develop AF is 26% and slightly less for a woman (23%).[1] Most adults develop AF later in life; the average age for men is 67, for women age 75.[1] In addition, the prevalence is greater for whites compared to blacks or other races.[1] However, blacks usually develop AF at a younger age.

Risk prediction models have been developed that identify risk factors for new-onset AF.[1] Table 1 displays the standard risk factors for AF. An interactive risk score calculator, from the Framingham Heart Study, is available for NPs at http://framinghamheartstudy.org/risk/atrial.html.

Table 1. Standard Risk Factors for Atrial Fibrillation (AF)

• Advanced age • Male sex • European ancestry • Body size (BMI ≥ 30 kg/m^2 or increased height) • Elevated SBP (≥ 160 mm Hg) or treatment for HTN • Prolonged PR interval (≥ 200 ms) • Diabetes • Presence of CVD (CHD, HF, or valvular heart disease) • Less common risk factors: hyperthyroidism (may be subclinical), chronic kidney disease, or heavy alcohol consumption

BMI = body mass index; CHD = coronary heart disease; CVD = cardiovascular disease; HF = heart failure; HTN = hypertension; SBP = systolic blood pressure.
Data from Go et al[1]*and Furie et al*.[2]

AF varies in presentation, from being asymptomatic to completely disabling. Yet, regardless of how asymptomatic a patient is, AF is associated with increased mortality and morbidity. AF nearly doubles a patient's risk of death (odds ratio of 1.5 for men; odds ratio of 1.9 for women) and increases the risk of ischemic stroke by 4-5, compared to those without AF.[1]However, the risk of stroke in patients with AF is quite variable, ranging from 1%-20% annually, depending on comorbidities, age, and history of previous stroke.[2] In addition, persons with AF are twice as likely to have dementia and more likely to develop heart failure (HF) (~40% of those with AF).[1]

Table 2. Classification of Atrial Fibrillation (AF)

Type of AF	**Characteristics**
Paroxysmal AF	Recurrent AF; lasting < 7 days (most < 24 hours); spontaneously returns to sinus rhythm without treatment
Persistent AF	Recurrent AF; lasting ≥ 7 days, requiring treatment to revert to sinus rhythm
Permanent AF	AF that is permanent; no treatment is able to restore sinus rhythm (cardioversion has failed or has not been attempted). Includes cases of long-standing AF (> 1 year)

Data from Lubitz et al[3]*and Fuster et al*.[4]

AF Classification

A variety of clinical and research classification schemes for AF have been used to inform clinical decision making, including schemes that classify AF based on etiology, pathophysiology, symptoms, temporal patterns, and quality of life.[3] Traditionally, most clinicians have classified AF as acute (lasting < 48 hours) versus chronic; however, new classification schemes have gradually led to disuse of these terms.[3] To be clinically useful, a temporal rhythm-based pattern classification should be used to characterize the type of arrhythmia at the time of presentation (at the moment the NP examines the patient).[4] The NP should distinguish whether the patient with AF has a first-detected (or first diagnosed) episode versus a recurrent episode (having 2 or more episodes) regardless of symptoms.[3,4] First detected AF may be further subclassified as

paroxysmal or persistent (Table 2) .[3,4] Likewise, recurrent episodes may be further subclassified as paroxysmal or persistent AF and may progress to permanent AF.[4]

Patients may have more than one type of AF over their lifetime. For example, an individual may have paroxysmal episodes lasting seconds or hours for years; then over time, as his or her atrium experiences electrical and mechanical remodeling from the AF, he or she may have more persistent episodes or develop permanent AF. Because patients may have more than one type of AF, they should be categorized by the most frequent type with which they present.[4]

Another term, "lone AF," has been used to apply to young patients (< 60) who have AF yet no clinical or echocardiographic evidence of heart or lung disease, including hypertension.[3,4] These patients generally have a more favorable diagnosis (in terms of mortality and risk of stroke or thromboembolism).[4] However, it is debatable whether the use of this term is appropriate as a distinct subset of AF because individuals with lone AF may also be classified as one of the subtypes of recurrent AF.[3] The remainder of this article will focus on the management of patients with recurrent AF (paroxysmal AF and persistent AF) and permanent AF.

Although the amount of time the patient spends in AF may differ, the increased risk of ischemic stroke is about the same for paroxysmal, persistent, or permanent AF.[1] Thus, nurse practitioners (NPs) need to remember that one of the most important treatment goals for all 3 types of chronic AF is to prevent stroke. Other major treatment goals are to control the ventricular heart rate (during episodes of AF) and restore sinus rhythm in persistent AF (in appropriate patients).

Rate Control

Reduction of the ventricular heart rate for patients in AF allows for adequate filling time to the ventricles and, in some cases, helps avoid rate-related ischemia.[5] However, the optimal ventricular heart rate has not been definitively determined.[5] Criteria for heart rate control are individualized but usually are between 60-80 beats per minute (bpm) at rest and 90-115 bpm during moderate levels of exercise.[5] The 2013 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) practice guideline (a compilation of the 2006 and 2011 recommendations for the management of patients with AF) indicates that there is no benefit to "strict rate control" (< 80 bpm at rest or < 110 bpm during a 6-minute walk), as opposed to "lenient rate control" (resting heart rate of < 110 bpm) in patients with stable persistent AF (left ventricular [LF] function > 0.40 and no or acceptable symptoms from the AF).[6]

Rate control for patients in AF is generally obtained by either the use of a beta-blocker or a non-dihydropyridine calcium channel blocker (CCB, primarily diltiazem or verapamil).[6] In addition, digoxin is effective for controlling heart rate at rest in patients with AF and concurrent HF or for sedentary individuals.[6] However, digitalis should not be the only medication used to control ventricular rate in patients with paroxysmal AF.[6] Some patients may require a combination of digoxin and either a beta-blocker or a nondihydropyridine CCB to control heart rate at rest and with exercise.[6] However, the dose of the combination therapy should be individualized to avoid bradycardia. If ventricular heart rate control does not offer symptomatic relief, then restoration of sinus rhythm becomes a treatment goal.[4]

Restoration of Sinus Rhythm

Not all patients with AF need to have sinus rhythm restored. For example, for patients who are not highly symptomatic or are elderly or generally sedentary, restoration of sinus rhythm is not generally needed. However, if a patient is highly symptomatic with recurrent AF, then maintenance of sinus rhythm to relieve symptoms may be required. However, maintaining sinus rhythm is a laudable goal in many. Early cardioversion may be necessary for patients with AF who have associated hypotension or worsening HF.[4]

When considering pharmacologic cardioversion, the NP should screen for and treat any precipitating or reversible causes of AF before starting antiarrhythmic drug therapy.[5]Examples of reversible (secondary) causes include metabolic disorders (eg, thyroid dysfunction), sleep apnea, excessive alcohol consumption or illicit drug use, or myocardial ischemia.

For patients who have been in AF for greater than 24-48 hours, it is important to make sure they have been adequately anticoagulated for 30 days before any attempts to restore sinus rhythm by cardioversion. For example, the international normalized ratio (INR) for patients on warfarin should be greater 2.0 for at least 2 weeks for 30 days before chemical or direct current cardioversion (DCCV). Likewise, patients who are on a newer antithrombotic agent (dabigatran [Pradaxa®], rivaroxaban [Xarelto®], and apixaban [Eliquis®]) should also stop taking these medications for at least 30 days before the attempt to restore sinus rhythm by chemical or DCCV. If it is unclear how long the patient has been in AF, a transesophageal echocardiogram may be necessary if the proper time for anticoagulation cannot be confirmed before restoring sinus rhythm by cardioversion.

Chemical cardioversion may be achieved by the administration of flecainide, dofetilide, propafenone, amiodarone, dronedarone, sotalol, or ibutilide.[4,5] Propafenone or flecainide is reasonable for patients with lone AF (no other risk factors or associated structural heart disease), if they are in sinus rhythm at the time of initiation.[6] Starting some antiarrhythmic medication (eg, amiodarone or dronedarone) as an outpatient is reasonable, based on the ACCF/AHA guideline, for patients without heart disease and when the agent is well tolerated. However, dofetilide and sotalol are more prone to cause QT prolongation and thus should be initiated in the hospital, where continuous telemetry monitoring, 12-lead electrocardiography (ECG), and laboratory monitoring are available to minimize the risk of QT prolongation and subsequent risk of Torsade de Pointes or sudden death. Thus, it is reasonable for NPs to make referrals to the cardiology team to choose an optimal antiarrhythmic medication and to discuss inpatient versus outpatient initiation of therapy before starting the medication.

Regardless of where therapy is started, rarely does antiarrhythmic medication totally eliminate AF. Having occasional recurrences, especially if they are self-terminating, is considered a good response to therapy. It is also reasonable for NPs to refer patients for catheter ablation, as an alternative to pharmacologic therapy, to treat symptomatic paroxysmal or persistent AF.[4,6]

Prevention of Stroke and Other Thromboembolic Events

Regardless of whether medication or ablation is used for rate or rhythm control, the need for antithrombotic therapy for stroke prevention is based on stroke risk, not whether the patient is in sinus rhythm. Moreover, the same criteria should be used regardless of the pattern (ie, paroxysmal, persistent, or permanent AF).[6] Thus, NPs need to evaluate every patient with AF, with the exception of those with lone AF or with contraindications, for the need for antithrombotic therapy.[6]

Assessing Stroke Risk in Patients with Chronic AF

Because antithrombotic agents are associated with bleeding risks, NPs should stratify the risk in patients to determine who, given the risks and benefits, are good candidates for these agents.[7] Research has shown that many patients who would benefit from stroke prevention do not always receive it. The ATRIA study found that approximately 55% of eligible insured patients with chronic AF who could have received warfarin for stroke prevention never got it.[7] The percentage was higher in patients who were uninsured or elderly.[7] However, placing all patients in AF on antithrombotic therapy is not advisable either, because the risk of major bleeding with these agents.

One risk-stratification tool recommended by the ACCF/AHA is the $CHADS_2$ scoring schema (Table 3). The $CHADS_2$ score takes into account the stroke risk factors for patients with AF and assigns 1-2 points for each risk factor. Each letter in the acronym stands for the condition or comorbidity that has been identified as a risk factor for stroke in patients with AF. A prior stroke or transient ischemic attack, the highest relative risk factor for developing a future stroke, earns a patient 2 points, as indicated by the "S_2" part of the acronym. Total $CHADS_2$ scores may range from 0 to 6, with higher total scores equating with a higher likelihood of stroke risk. Patients with scores of 0-1 have a relatively low stroke risk, whereas, patients with the maximum score (6) have the highest risk of stroke.[8]Table 4displays the adjusted annual stroke risk based on $CHADS_2$ score.

Table 3. Calculating Stroke Risk Using the $CHADS_2$ Scoring Schema

Risk Factor	**Points**
Congestive heart failure[a]	1
Hypertension (or treated hypertension)	1
Age older than 75 years	1
Diabetes	1
Prior **S**troke or transient ischemic attack	2

a. The term *congestive heart failure* is being replaced by many clinicians with *cardiac heart failure*.
Data from Furie et al.[2]

A second, more refined risk stratification instrument, the CHA_2DS_2 VAS_c scoring schema, adopted by the European Society of Cardiology, may generate scores ranging from 0 to 9. As with the $CHADS_2$ scores, higher scores indicate a higher stroke risk. This scoring instrument includes additional risk factors for stroke into the total score, assigning points for congestive HF,

hypertension, age > 75 (2 points instead of 1), diabetes, stroke (2 points), vascular disease, age 65-74 (1 point), and a sex category (being female).[9] The inclusion of age 65-74, female gender, and vascular disease identifies at-risk patients who would not have been identified with the $CHADS_2$ scoring schema.

Table 4. Adjusted Annual Stroke Risk (Based on $CHADS_2$ Score)

$CHADS_2$ Score	**Annual Stroke Risk**
0	1.2%-3%
1	2%-3.8%
2	3.1%-5.1%
3	4.6%-7.3%
4	6.3%-11.1%
5	8.2%-17.5%
6	10.5%-27.4%

Data from Gage et al.[8]

Stroke Prevention for Patients with Nonvalvular AF

Regardless of the $CHADS_2$ score, patients who have significant valvular heart disease or an artificial heart valve need chronic antithrombotic therapy, specifically warfarin. Treatment recommendations for patients with nonvalvular AF (patients without significant valvular heart disease, an artificial valve, or mitral valve repair) vary, however, depending on the $CHADS_2$ score for the individual patient.

The American College of Chest Physicians guideline on antithrombotic therapy, published annually, offers recommendations for antithrombotic stroke prophylaxis for patients with nonvalvular AF[10] (Table 5). Based on these recommendations, patients with a $CHADS_2$score of 0 (low stroke risk) should not be treated with antithrombotic therapy. For those patients who prefer therapy, it is recommended that aspirin alone or a combination of aspirin and clopidogrel be used.[10] For patients with a $CHADS_2$ score of 1, oral antithrombotic therapy is recommended, as opposed to no therapy, aspirin alone, or the combination of aspirin and clopidogrel. However, which antithrombotic agent is chosen may be individualized.[10] Patients with a $CHADS_2$ score of > 2 should receive antithrombotic therapy, unless contraindicated, which may include warfarin or one of the newer antithrombotic agents discussed below.

Table 5. Treatment Recommendations Stroke Prevention Based on $CHADS_2$ Score

$CHADS_2$Score	**Stroke Risk**	**Treatment Recommendation**
0	Low	No therapy. If therapy is chosen, aspirin
1	Moderate	Oral antithrombotic therapy is recommended over aspirin or the combination of aspirin/clopidogrel
≥ 2	High	Oral antithrombotic therapy

Data from You et al.[10]

Current Antithrombotic Agents

Vitamin K Antagonists

Warfarin, a vitamin K antagonist, is relatively inexpensive and, until recently, was considered the best agent to prevent stroke in patients with AF. However, warfarin has 2 disadvantages: underutilization and difficulty in maintaining the serum blood level (ie, PT/INR) in a desired therapeutic range. Patients who have a subtherapeutic range are at an increased risk for thromboembolic events, whereas patients with INR levels above the therapeutic range are at increased risk for bleeding. Moreover, the inconvenience of dose titration and monitoring serum levels is burdensome for patients and providers.

New Antithrombotic Agents

Three alternative antithrombotic agents to warfarin have recently been approved by the Food and Drug Administration: dabigatran, rivaroxaban, and apixaban. These agents are approved for patients with nonvalvular AF. If chronic anticoagulation is needed for those patients, warfarin should be used (unless contraindicated).

Common characteristics of the new agents are that they peak fairly quickly (2-4 hours), have shorter half-lives (5-12 hours), are out of the body sooner if discontinued (within a few hours, unless there is renal impairment), and have fewer drug-drug interactions compared to warfarin.[11] In addition, the newer agents do not require dose titration or lab monitoring once started. However, a disadvantage of the newer agents is that they do not have an antidote for reversal, as is the case for warfarin.

A recent indirect comparison of all 3 agents (used in nonvalvular AF patients) found that they offer an advantage of fewer strokes and systemic emboli and provide an addition 10% reduction in mortality.[11] In addition, all 3 agents were associated with lower bleeding rates (including fewer hemorrhagic strokes, intracranial hemorrhages, and major bleeds) compared to warfarin.[11] Refer to Table 6 for a comparison of all 4 antithrombotic agents.

Table 6. Antithrombotic Treatment Options for Stroke Prevention in Nonvalvular AF

Agent/Action	Dosing Information	Drug-Drug or Drug-Food Interactions	Management of Bleeding	Key Implications for NPs
Warfarin (Coumadin®) Vitamin K Antagonist	Peak effect: 72-96 hours Half-life: 40 hours Typically starting dose between 2 to 5 mg once daily, in the evening No dosage adjustment with kidney impairment	Many drug-drug and drug-food interactions	Antidote: Vitamin K Concurrent use with other agents that alter coagulation factors (eg, aspirin, antiplatelet agents, chronic NSAID use, heparin, fibrinolytics) ↑ bleeding risk	Requires ongoing lab monitoring. INR goal: 2.0-3.0 (higher if mechanic valve)

Agent/Action	Dosing Information	Drug-Drug or Drug-Food Interactions	Management of Bleeding	Key Implications for NPs
Dabigatran (Pradaxa®) Direct Thrombin Inhibitor (Factor IIa inhibitor)	Peak effect: 2-3 hours Half-life: 12-17 hours Primarily eliminated by the kidneys Dose: 150 mg twice daily (for CrCl > 30 mg/mL) 75 mg twice daily (for CrCl 15-30 mg/mL) *Contraindicated if CrCl < 15 mL/min	Drug-food interactions: None known. Take with or without food Drug-drug interactions: Concurrent use with inducers of CYP3A4 & P-gp (eg, rifampin, carbamazepine, phenytoin, St. John's wart) ↓ exposure to the drug (↑ stroke risk). Co-administration of rifampin and dabigatran should be avoided Concurrent use of strong inhibitors of CYP3A4 & P-gp (eg, ketoconazole, itraconazole, ritronavir, clarithromycin) ↑ bleeding risk. Dose of agent should be ↓ (75 mg bid) if given to patients with moderate kidney impairment (CrCl of 30-50 mL/min) and if given with dronedarone or systemic ketoconazole	No specific antidote. Concurrent use with other agents that alter coagulation factors (eg, aspirin, antiplatelet agents, chronic NSAID use, heparin, fibrinolytics) ↑ bleeding risk Minor bleeds: temporary discontinuation of agent Major bleeds: Stop the agent, apply direct pressure to compressible sites, give IV fluids and blood products (FFP 2-4 units, RBCs, or prothrombin complex concentrate) Activated prothrombin complex or recombinant Factor VIIa 90 mcg/kg may be helpful Dabigatran is partially dialyzable. Oral/liquid activated charcoal may be considered for cases of overdose	Requires no lab monitoring. Patient must be able to swallow capsules. Do not open, cut, or crush capsules Do not pre-fill pill containers Advise patients to open blister packs just before taking medication. Use all capsules within 4 months of opening bottle Advise patients if they miss a dose, can take the missed dose if spaced out by ≥ 6 hours. Otherwise, don't double doses
Rivaroxaban (Xarelto®) Direct factor Xa inhibitor	Peak effect: 2-4 hours Half-life: 5-9 hours (healthy adults age 2-45 years); 11-13 hours for elders or those with CKD Partially eliminated by the kidneys (~ 33%) Dose: 20 mg daily (for CrCl ≥ 50 mg/mL) 15 mg daily (for CrCl 15-49	Drug-food interactions: (for 15 or 20 mg dose): take *with food* (the evening meal) to maximize bioavailability Drug-drug interactions: Concurrent use with inducers of CYP3A4 & P-gp (eg, rifampin, carbamazepine, phenytoin, St. John's wart) ↓ exposure to the drug (↑ stroke risk). Co-administration of these agents should be *avoided*	No specific antidote. Concurrent use with other agents that alter coagulation factors (eg, aspirin, antiplatelet agents, chronic NSAID use, heparin, fibrinolytics) ↑ bleeding risk Minor bleeds: temporary discontinuation of agent Major bleeds: same as dabigatran, except this agent is not dialyzable Oral/liquid activated	Requires no lab monitoring Take with food (evening meal) If unable to swallow the tablet, it may be crushed and taken with a small amount of applesauce, followed by food Tablet may be crushed and mixed with

Agent/Action	Dosing Information	Drug-Drug or Drug-Food Interactions	Management of Bleeding	Key Implications for NPs
	mg/mL) *No dosing information if CrCl < 15 mL/min or if on dialysis	Concurrent use of strong inhibitors of CYP3A4 & P-gp (eg, ketoconazole, itraconazole, ritronavir, clarithromycin) ↑ bleeding risk. *Avoid* concomitant use with any of these agents with rivaroxaban	charcoal may be considered for cases of overdose	water if administered through an NG or gastric feeding tube
Apixaban (Eliquis®) Direct factor Xa inhibitor	Peak effect: 3-4 hours Half-life: 12 hours Partially eliminated by the kidneys (~27%) Dose: 5 mg twice daily 2.5 mg twice daily if at least 2 of the following: age ≥ 80 years, body weight of ≤ 60 kg, or serum creatinine of ≥ 1.5 mg/dL *Contraindicated if CrCl < 25 mL/min	Drug-food interactions: None known. Take with or without food Drug-drug interactions: Concurrent use with inducers of CYP3A4 & P-gp (eg, rifampin, carbamazepine, phenytoin, St. John's wart) ↓ exposure to the drug (↑ stroke risk). Co-administration of these agents should be *avoided* Concurrent use of strong inhibitors of CYP3A4 & P-gp (eg, ketoconazole, itraconazole, ritronavir, clarithromycin) ↑ bleeding risk. If any concurrently administered, a *lower dose* of apixaban should be prescribed (2.5 mg daily)	No specific antidote Concurrent use with other agents that alter coagulation factors (eg aspirin, antiplatelet agents, chronic NSAID use, heparin, fibrinolytics) ↑ bleeding risk Minor bleeds: temporary discontinuation of agent Major bleeds: same as dabigatran, except this agent is not dialyzable Oral/liquid activated charcoal may be considered for cases of overdose	Requires no lab monitoring Advise patients to take any missed dose as soon as possible on the same day it was originally scheduled. Do not double up on a missed dose if noted the next day

CKD = chronic kidney disease; CrCl = creatinine clearance; FFP = fresh frozen plasma; INR = international normalized ratio; NG = nasogastric; NSAID = nonsteroidal anti-inflammatory drug; RBCs = red blood cells.

Data from Boehringer Ingelheim Pharmaceuticals, Inc[12]; *Janssen Pharmaceuticals, Inc*[13]; *Bristol-Myers Squibb Pharma Co*[14]; *and Bristol-Myers Squibb Co.*[15]

Contraindications to Chronic Antithrombotic Therapy

Contraindications to antithrombotic therapy include active bleeding or the potential for major bleeding, which include blood dyscrasias, recent or anticipated surgery of the central nervous

system, spinal puncture or other diagnostic or therapeutic procedures that have the potential for uncontrollable bleeding, major regional/lumbar block anesthesia, a known hypersensitivity to any agent under consideration, malignant hypertension, and unsupervised patients who have the high potential for nonadherence.[12-15]

In addition, patients who should not receive the newer antithrombotic agents include those with prosthetic valves, hemodynamically significant valvular heart disease, severe kidney failure (eg, creatinine clearance < 15 mL/min), or advanced liver disease (eg, impaired baseline clotting function).[12-14] Pregnant women (with the exception of those who have mechanical heart valves) should not be prescribed warfarin.[15] Furthermore, per the packet inserts, pregnant or breastfeeding women should not receive the newer antithrombotic agents.[12-14]

For patients who have contraindications to long-term antithrombotic therapy, NPs should consider referral for consideration for left atrial appendage closure to reduce the risk of stroke.[16] Discussion of contemporary treatment advances in stroke prevention for this special population is beyond the scope of this article; however, NPs should know that options exist.[16]

Table 7. Comparison of Bleeding Risk Scores: HEMORR$_2$HAGES and HAS-BLED

Scoring Schema	Bleeding Risk	Calculation of Bleeding Risk Score
HEMORR$_2$HAGES	Low risk: 0-1 points Moderate risk: 2-3 points High risk: ≥ 4 points	*1 point for each (except as noted):* **H**epatic or kidney disease **E**thanol abuse **M**alignancy **O**lder age (> 75) **R**educed platelet count or function **R**e-bleeding risk (prior bleed) = **2 points** **H**ypertension (uncontrolled) **A**nemia **G**enetic factors (CYP2C9 polymorphisms) **E**xcessive fall risk **S**troke
HAS-BLED	Low risk: 0 points Moderate risk: 1-2 points High risk: ≥ 3 points Maximum score: 9 points	*1 point for each (except as noted):* **H**ypertension (uncontrolled) **A**bnormal kidney or liver function (1 point *each*) **S**troke **B**leeding history or predisposition **L**abile INR **E**lderly (age > 65) **D**rugs (concomitant use of antiplatelet/nonsteriodal anti-inflammatory drug) or alcohol (1 point *each*)

Data from You et al.[10]

Safety Concerns of Antithrombotic Agents

Bleeding Risks

The primary safety concern for any antithrombotic agent is major bleeding, which may be classified as a fatal or a nonfatal bleed (ie, hemorrhagic stroke, intraocular bleed, and gastrointestinal bleed). However, NPs should keep in mind that all of these bleeding events combined occur infrequently (~2-4% per year) for any of the antithrombin agents discussed (warfarin, dabigatran, rivaroxaban, or abixaban).[11] In fact, the risk of hemorrhagic stroke, one of the most worrisome types of non-fatal bleeds, occurs ~0.10%-0.47%/year, less so with the newer agents (0.10%-0.26%/year).[11]

Despite the decreased likelihood of major bleeding with the use of any antithrombotic agent, NPs should assess the bleeding risk for their patients. Some NPs use bleeding risk scores (eg, HEMORR$_2$HAGES or HAS-BLED) to evaluate the likelihood of bleeding (Table 7).[17,18] These risk scoring schemas, however, are based on research done on warfarin. NPs need to keep in mind that some of the risk factors serve as an absolute or a relative contraindication to starting therapy (eg, a history of bleeding [the greatest risk factor], abnormal liver or kidney disease, uncontrolled hypertension, concomitant drug or alcohol use, reduced platelet count/function, excessive fall risk, and malignancy).[12-15]Other risk factors for bleeding, however, are also risk factors for having a stroke (eg, prior history of stroke, age > 65 years, and a history of hypertension).[10] In fact, the likelihood of bleeding is higher if the patient has a higher CHADS$_2$ score.[19] However, NPs need to keep in mind that the chances of a stroke are higher in these patients than the chances that they may bleed. Thus, the likelihood of stroke takes priority over the likelihood of bleeding in patients with AF.

Bleeding Management

One of the considerations when prescribing antithrombotic therapy relates to how bleeding is managed. Since the newer agents have a relatively short half-life, compared to warfarin, temporary discontinuation of therapy may be sufficient in stopping any minor bleeds related to dabigatran, rivaroxaban, or apixaban. All 3 of the newer agents should be discontinued at least 24-48 hours before elective surgery or invasive procedures that have a moderate to high risk of clinically significant bleeding.[12-14] Longer drug-free intervals, 3 to 5 days, should be considered for patients who have an altered kidney function.[12-14] After surgery, the medications may be resumed when hemostasis is obtained to avoid too long of a drug-free interval, placing the patient at risk for stroke.[12-14] However, the packet insert and the surgeon should be consulted to discuss specific patient situations.

For major bleeds, warfarin has a specific antidote (vitamin K). While there are no specific antidotes for the newer antithrombotic agents, universal antidotes for factor Xa inhibitors (eg, rivaroxaban and apixaban) are currently in phase 2 drug development studies.[20] See Table 6 for the treatment of major bleeding related to the antithrombotic agents discussed.

Patient Education

NPs should educate all patients with AF to notify their provider should they have new or worsened symptoms. Patients should also be instructed to monitor for signs and symptoms of bleeding related to antithrombotic therapy (eg, unusual bleeding from nose or gums, heavier than normal menstrual bleeding, red or brown urine, red or black stools, hemoptysis, vomiting blood or coffee ground emesis, or unusual bruising or discoloration on the skin) and to seek help should any of these situations arise.

In addition, NPs should provide counseling about the importance of not missing a dose of any medications and avoiding abrupt discontinuation of any medication (especially the new antithrombotic agents, as this places patients at an increased risk of stroke). If a patient is prone to miss an occasional dose of anti-thrombotic therapy, it is better for the NP to place him or her on warfarin because of a longer half-life, allowing some "coverage" for stroke prevention, compared to the newer agents. Regardless, patients should be instructed to contact their health care provider should they want to stop their medications for any reason.

Educational resources are available to NPs and their patients with AF, including resources from the American Association of Nurse Practitioners, the National Institutes of Health, the Heart Rhythm Society, the American Association of Heart Failure Nurses, the National Stroke Association, and the Preventive Cardiovascular Nurses Association (Table 8).

Table 8. Educational Materials for NPs and Patients With Atrial Fibrillation

American Association of Nurse Practitioners http://www.aanp.org/education/51-education/education-toolkits/1210-heart-matters
National Institutes of Health http://www.nlm.nih.gov/medlineplus/tutorials/atrialfibrillation/htm/index.htm
Heart Rhythm Society http://www.hrsonline.org/Patient-Resources/Heart-Diseases-Disorders/Atrial-Fibrillation-AFib#axzz2YnS7AZoV
American Association of Heart Failure Nurses http://www.aahfnpatienteducation.com/index.php/atrial_fibrillation
National Stroke Association http://www.stroke.org/site/DocServer/AFIB_toolkit_web_sm.pdf
Preventive Cardiovascular Nurses Association http://pcna.net/patients/atrial-fibrillation

Conclusion

NPs need to provide guideline-directed medical therapy for their patients with AF. Treatment goals should include control of the ventricular heart rate, prevention of stroke and systemic embolism, and maintenance of sinus rhythm for some individuals. NPs should conduct risk stratification for patients with AF to determine who needs stroke prophylaxis. For those patients who need therapy, new treatment options are available. NPs need to weigh the pros and cons of using new therapy versus conventional treatment with warfarin to optimize patient outcomes. NPs should also err on starting chronic antithrombotic therapy in an effort to prevent stroke.

Finally, NPs should make referrals to appropriate support services and empower their patients to be engaged in self-care.

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Vitae

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