dialogues IN CLINICAL PRACTICE

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Improving Quality of Life in Patients With Atrial Fibrillation Through Safer, More Individualized Treatment Approaches

COMPLIMENTARY CME

In May 2012, Med-IQ convened a roundtable meeting to discuss strategies for individualizing patient care in atrial fibrillation (AF). Faculty experts explored the strengths and limitations of the current AF classification system and discussed factors that predict AF progression. The expert panel also discussed clinical decision making regarding treatment strategies in pursuing rate and rhythm control as well as patient- and clinician-related barriers to optimal AF management. This publication presents key topics explored during the roundtable and includes excerpts from the discussion.

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NOTE: If you are accessing this guide online and have already answered these pre-survey questions electronically, you may skip this step and proceed to the activity.

1. How confident are you in your ability to select the most appropriate guideline-recommended therapy for your patients with AF?

A. Extremely confident
B. Moderately confident
C. Somewhat confident
D. Not confident at all

2. How confident are you in your ability to determine whether a patient with AF is an appropriate candidate for catheter ablation?

A. Extremely confident
B. Moderately confident
C. Somewhat confident
D. Not confident at all

3. Have you ever provided a medication log to your patients with AF to track their medication adherence?

A. Yes
B. No

4. Based on the HATCH score, which of the following patients with paroxysmal AF would be most likely to progress to persistent or permanent AF?

A. A 68-year-old man with a history of stroke and heart failure
B. A 70-year-old man with hypertension and heart failure
C. A 73-year-old man with COPD and a history of stroke
D. A 76-year-old man with hypertension and COPD
E. I am unfamiliar with the HATCH score

5. Guidelines advise that the selection of an antiarrhythmic agent for patients with AF should primarily be driven by:

A. Efficacy
B. Safety
C. Patient preference
D. Tolerability of side effects

6. Which of the following statements about catheter ablation is TRUE?

A. The highest cure rates can be expected in patients with paroxysmal AF and a structurally normal heart
B. Treatment-naïve patients with recently diagnosed AF are optimal candidates
C. It should not be considered as an option for patients with symptomatic paroxysmal AF who have LV dysfunction
D. Longer-term follow-up studies suggest than more than 30% of patients remain arrhythmia free after a single procedure at 5 years

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CME Information

Target Audience
This activity is intended for cardiologists and electrophysiologists.

Series Overview/Statement of Need
Atrial fibrillation (AF) is the most frequently diagnosed arrhythmia in clinical practice, affecting more than 6 million people in the US. Suboptimal management of this condition is associated with increases in hospitalizations, healthcare costs, and even mortality and results in decreased patient quality of life. Contemporary AF management strategies vary widely; this reality is related to a lack of definitive expert consensus on effective treatment strategies, an underappreciation of the clinical significance of AF, and a lack of emphasis on individual patient factors when designing treatment plans. Deviations from guidelines, emergence of new drugs, multiple recent guideline updates, and suboptimal patient adherence create a significant need for education on current evidence and best practices for managing this complex disease.

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Kenneth A. Ellenbogen, MD, has indicated no real or apparent conflicts.

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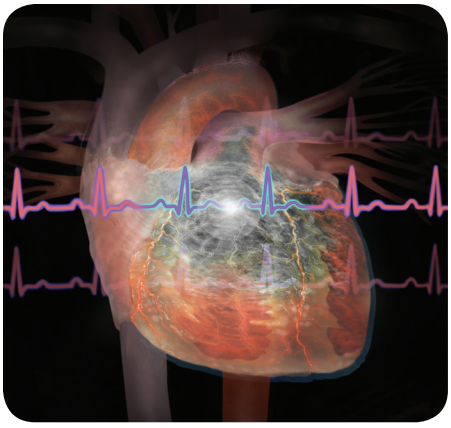

Learning Objectives

Upon completion, participants should be able to:

- Describe the potential contribution of patient factors and adherence on the progression of AF and disease-related outcomes, and employ strategies to address these factors
- Identify available pharmacologic treatment options for rate and rhythm control in patients with AF, and discuss how their respective safety and efficacy profiles factor into the development of individualized care plans
- Assess current evidence regarding appropriate candidates, short- and long-term efficacy and safety, and optimal sequencing of catheter ablation for the management of AF

ROUNDTABLE MEETING

In May 2012, Med-IQ convened a roundtable meeting to discuss strategies for individualizing patient care in atrial fibrillation (AF). Roundtable experts included the following:

Kenneth A. Ellenbogen, MD: Dr. Ellenbogen is Chairman of the Division of Cardiology at Pauley Heart Center and Director of Clinical Cardiac Electrophysiology & Pacing at Medical College of Virginia and McGuire Veterans Administration Medical Center (VAMC). Dr. Ellenbogen is a Fellow of the American College of Cardiology, the Council on Clinical Cardiology, and the Council on Circulation of the American Heart Association. Dr. Ellenbogen's academic, clinical, and research interests include newer, more effective ways to perform ablation and to develop methods for ablation in AF.

Gerald V. Naccarelli, MD: Dr. Naccarelli is the Bernard Trabin Chair in Cardiology, Professor of Medicine, Chief of the Division of Cardiology, and Director of the Cardiovascular Center at the Pennsylvania State University College of Medicine/Milton S. Hershey Medical Center. Dr. Naccarelli's research interests are in AF, clinical arrhythmia trials, implantable devices for treating arrhythmias and congestive heart failure, antiarrhythmic drug development, and autonomic aspects of arrhythmogenesis.

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Oussama M. Wazni, MD: Dr. Wazni is Staff Physician in the Cleveland Clinic Section of Cardiac Electrophysiology and Pacing as well as the Electrophysiology Labs Director. He is board certified in internal medicine, cardiology, and cardiac electrophysiology. Dr. Wazni is on the editorial board of the *Journal of the American College of Cardiology* and the *Journal of Cardiovascular Electrophysiology*. He specializes in electrophysiology with special interest in AF and ventricular tachycardia ablation.

Together, these experts explored the strengths and limitations of the current AF classification system and discussed factors that predict AF progression. They also discussed clinical decision making regarding treatment strategies in pursuing rate and rhythm control in patients with AF and examined common patient- and clinician-related barriers to optimal AF management.

This print publication presents key topics from the roundtable and includes text excerpts from the discussion. The online version of this publication, available at www.Med-IQ.com/a666, is further enhanced with audio clips from the roundtable discussion. We have placed boxes throughout this print publication to indicate when additional audio content is available online. Please note: the audio content in the online version is designed to supplement this print publication and, therefore, is not factored into the estimated time to complete this activity.

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If not, please complete the pre-survey on page 2 before continuing.

INTRODUCTION

AF is the most frequently diagnosed arrhythmia in clinical practice and affects an estimated 6 million people in the United States (US).[1] The lifetime risk of developing AF is 1 in 4 for adults age 40 years and older, and prevalence is expected to increase over the coming decades as the population ages.[1,2] AF is not a benign condition; its symptoms can be disabling, it substantially increases the risk of stroke, and it doubles the risk of death related to stroke.[2] Hospitalizations due to AF account for one-third of all admissions for cardiac arrhythmias.[3] Moreover, persistent and permanent forms of AF contribute to structural changes to the atria and possibly the ventricles that further increase symptomatology and stroke risk.[3]

Clinical decision making in AF management relies heavily on individual patient characteristics. Despite the availability of practice guidelines and treatment algorithms, developing an optimal management strategy is not always a straightforward process.

CLASSIFICATION AND PROGRESSION OF AF

Several classification schemes for AF have been proposed. Agreed-upon definitions of different types of AF are useful in guiding general approaches to therapy, standardizing research protocols, and facilitating communication among healthcare professionals and researchers. The joint 2006 American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) Guidelines for the Management of Patients With Atrial Fibrillation offer the following definitions of AF[3]:

- **Paroxysmal AF:** at least 2 episodes (usually less than 24 hours' duration) of AF that terminate spontaneously within 7 days; may be recurrent
- **Persistent AF:** continuous AF that is sustained beyond 7 days; may be recurrent
- **Long-standing persistent AF:** continuous AF of greater than 12 months' duration
- **Permanent AF:** an arbitrary definition in which AF is uninterrupted and cardioversion is not attempted or has failed

Over time, patients may alternate between paroxysmal and persistent AF classifications.[3] For example, a patient with paroxysmal AF may have occasional episodes of persistent AF. Guidelines recommend categorizing patients using the most frequently occurring AF presentation.[3]

It has been estimated that approximately 82% of patients with AF are 65 years or older and that 37% are 80 years or older.[4] Not surprisingly, these patients often have comorbid cardiovascular disease (CVD), such as hypertension, coronary artery disease, congestive heart failure, or valvular disease.[3] Population-based studies suggest that fewer than 12% of AF cases occur in patients younger than 60 years of age who do not have a history of comorbid CVD (including hypertension); other studies, however, have found this figure to exceed 30% of cases. This presentation is sometimes referred to as "lone AF." The risk of stroke and mortality appears to be lower in these patients. As they age, however, such patients can develop CVD that contributes to the progression of AF.[3]

AF is considered to be a self-propagating, progressive disorder.[5] Over a period of years, the majority of patients with paroxysmal AF and comorbid CVD will progress to persistent AF; only 2% to 3% of patients will remain in paroxysmal AF over several decades.[2] Current research suggests that a substantial number of patients with paroxysmal AF will progress to persistent AF within 1 year of diagnosis. In an analysis of data from 1,219 patients with paroxysmal AF (average age of 64 ± 13 years) participating in the Euro Heart Survey on AF, progression occurred in 15% of patients within 12 months.[6] Based on the patient characteristics of this population, researchers developed a risk stratification schema that allowed for reliable and immediate classification of the risk of progression to persistent or permanent AF in patients with paroxysmal AF. The so-called HATCH score is calculated based on the following independent factors that predict AF progression[6]:

- **H**ypertension (1 point)
- **A**ge > 75 years (1 point)
- **T**ransient ischemic attack or stroke history (2 points)
- **C**hronic obstructive pulmonary disease (1 point)
- **H**eart failure history (2 points)

Approximately 50% of patients with a baseline HATCH score of more than 5 experienced AF progression after 1 year compared with only 6% of the patients with a HATCH score of 0.[6]

Progression is less likely in patients with lone AF. A recent observational study of 346 patients newly diagnosed with lone AF confirmed the relatively benign course in this population.[7]

Roundtable Perspective: Advantages and Limitations of the ACC/AHA/ESC Classification System

Dr. Ellenbogen: *The definitions of AF based upon guideline documents are reasonable definitions so that we can communicate with one another. The main limitation is that they do not incorporate in any way the burden of AF. There are people who have paroxysmal AF who are completely asymptomatic, others who have one 15-minute episode every 6 months, and others who have daily 15-minute episodes where they are completely miserable. The definitions fail to reflect the burden of AF or patient quality of life. This is a shortcoming, and we must be careful to define the patients we are talking about treating.*

Dr. Reiffel: *The classification system is helpful in guiding general approaches to patients. For example, patients with paroxysmal AF don't require cardioversion, patients with persistent AF are often candidates for cardioversion, and patients with permanent AF are no longer candidates for pursuing sinus rhythm.*

The system is not particularly useful in issues related to anticoagulation because all AF patients require consideration of anticoagulation. Another problem is that AF episodes that last 2 minutes twice a year or that last 18 hours every day are both defined as paroxysmal AF. Implications for symptoms and risks must be different, but we don't know where that threshold is.

None of the classification systems tell us anything about different mechanisms of AF. There are some correlations mechanistically across the board in the absence of structural disease. For example, paroxysmal AF usually requires triggers, most often located in the pulmonary veins. The fact that it doesn't persist has some implications for the relative freedom from diseased substrate in contrast to conditions where the arrhythmia can persist.

Over a mean follow-up period of 12.1 years, approximately 27% of those with a confirmed diagnosis of paroxysmal AF converted to permanent AF. Older age and the development of congestive heart failure were predictive of AF progression (both $P < 0.01$), which, in turn, was a predictor of adverse outcomes, including thromboembolism, on multivariate analysis ($P < 0.05$).[7]

It is widely accepted that "AF begets AF" through electrical and structural remodeling and alterations in atrial contractile processes.[5] Electrical remodeling of the atria occurs within several days of persistent AF and involves changes in the atrial refractory period, including a shortening in duration and a loss of physiologic rate dependence. Atrial contractile remodeling also occurs rapidly and, over months to years, can lead to atrial dilatation and an increased risk of thrombus formation. Atrial enlargement can also result in further alteration of electrophysiologic properties and the propagation of multiple atrial wavelets.[5] Underlying anatomic and electrophysiologic alterations of the atrial substrate from CVD and aging are the most important factors determining AF progression.[5,8]

CHANGING PARADIGMS IN AF MANAGEMENT

The general treatment goals of AF include preventing thromboembolism, relieving symptoms, and improving survival.[2,3] Initial treatment and maintenance strategies are determined based on the following factors[2,3]:

- Type, frequency, and duration of AF
- Patient age
- Severity of symptoms
- Presence and severity of CVD and other select comorbidities (such as diabetes)
- Risks and benefits of therapy (nonpharmacologic and pharmacologic)

RISK STRATIFICATION

All types of AF carry an increased risk of stroke; the condition itself increases this risk up to 2- to 7-fold compared to individuals with normal sinus rhythm.[3] It is estimated that at least 20% of all strokes in the US are attributable to AF, and the risk of stroke in patients with AF increases markedly with age.[3] Additionally, AF-associated ischemic stroke is often more severe than stroke due to other causes.[2] Asymptomatic, unrecognized AF may also be attributed to some "cryptogenic" strokes.[2] Anticoagulation strategies should be based on thromboembolic risk stratification.[2,3]

The widely adopted $CHADS_2$ scoring system allows for rapid thromboembolic risk categorization and incorporates the following risk factors and assigned points[9]:

- **C**ongestive heart failure (1 point)
- **H**ypertension (1 point)
- **A**ge ≥ 75 years (1 point)
- **D**iabetes (1 point)
- Previous **S**troke or transient ischemic attack (2 points)

The modified CHA_2DS_2-VASc scoring system was developed to extend the predictive value of the $CHADS_2$ score and increase specificity at the lower end of the risk continuum.[10] It assigns 1 point for other vascular diseases (eg, previous myocardial infarction, peripheral artery disease, and aortic plaque), age 65 to 74 years, and female sex. It reclassifies an age of 75 or older to 2 points. Therefore, this scoring system may better classify patients with low or moderate risk.[10]

Table 1 summarizes oral anticoagulation recommendations from the 2011 ACCF/AHA/HRS Focused Update and the 2012 Science Advisory from the AHA and American Stroke Association (ASA) that incorporated newly available antithrombotic agents.[3,11,12] The selection of a particular agent should be based on patient-specific factors.[14]

In addition, the American College of Chest Physicians

TABLE 1. AHA/ASA- and ACCF/AHA/HRS-Recommended Anticoagulation in AF According to Risk

RISK CATEGORY	RECOMMENDED THERAPY
No risk factors	Aspirin 81-325 mg/day
1 moderate-risk factor	Aspirin 81-325 mg/day or warfarin (INR 2.0-3.0, target 2.5); dabigatran[a] or apixaban[b] are reasonable alternatives to warfarin; apixaban[b] is a reasonable alternative to aspirin in patients who cannot tolerate warfarin
≥ 1 high-risk factor or ≥ 2 moderate-risk factors	Warfarin (INR 2.0-3.0, target 2.5) or dabigatran; dabigatran[a], apixaban[b], or rivaroxaban[c] are reasonable alternatives to warfarin; dual antiplatelet therapy with aspirin/clopidogrel[d] may be considered in patients who cannot tolerate warfarin

HIGH RISK FACTORS	MODERATE RISK FACTORS	WEAKER/LESS VALIDATED RISK FACTORS
• Previous stroke, TIA, or embolism • Mitral stenosis • Prosthetic heart valve	• Age ≥ 75 years • Hypertension • Heart failure • Diabetes • LVEF ≤ 35%	• Female sex • Age 65-74 years • Coronary artery disease • Thyrotoxicosis

[a]Dabigatran is not recommended for patients with a CrCl of < 15 mL/min.
[b]As of the publication of this paper in August 2012, apixaban is an investigational agent. Apixaban should not be used in patients with a CrCl of < 25 mL/min.
[c]Rivaroxaban should not be used in patients with a CrCl of < 15 mL/min.
[d]Note that clopidogrel is not FDA approved for this indication; such use is off label.
INR = international normalized ratio; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.
Data derived from Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2011;57(2):223-242; Furie KL, Goldstein LB, Albers GW, et al. Oral antithrombotic agents for the prevention of stroke in nonvalvular atrial fibrillation: a science advisory for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2012;43:Epub Aug 2.

(ACCP) updated their guidelines for the prevention of AF-related thrombosis in 2012.[3] These recommendations largely align with those endorsed by the associations mentioned previously, with the key exception that the ACCP prefers dabigatran to adjusted-dose vitamin K antagonist therapy when oral anticoagulation is indicated.[3]

Beyond anticoagulation, the choice of AF management strategy involves deciding whether long-term rate or rhythm control should be attempted. Guidelines recommend the following[3]:

- No rhythm-control treatment is required in paroxysmal AF unless significant symptoms are present
- Rate control should also be a first step in persistent AF; antiarrhythmic therapy should be considered in appropriately selected patients
- If persistent AF is accepted as permanent, rate control should be offered as needed

Acutely, rate control is always essential, and drug therapy is needed except in those with slow rates due to atrioventricular-node (AVN) disease, high vagal tone, or the effect of drugs (eg, beta blockers and calcium-channel blockers) already being used for other purposes (such as hypertension).

The severity of symptoms often determines whether rate or rhythm control should be pursued. Symptoms can range from clinically "silent" AF to disabling palpitations, anxiety, dyspnea, chest pain, fatigue, and dizziness.[2,15] If patients are experiencing symptoms that interfere with their quality of life, the restoration of sinus rhythm may dramatically improve their functional status.[3]

Roundtable Perspective: The Role of Symptom Severity in Choosing a Maintenance Therapy

Kenneth A. Ellenbogen, MD
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Listen Now

Rate vs. Rhythm Control

Prospective randomized trials suggest that rate and rhythm control can result in similar survival outcomes.[16] The AFFIRM trial enrolled more than 4,000 patients (mean age of 70) with AF and a high risk of stroke or death.[17] Patients were randomly assigned to receive an anticoagulant and either antiarrhythmic medication (more than two-thirds of patients received amiodarone) or AVN-blocking medication to control ventricular rate without attempting to control rhythm. Results of this study indicated that there was no significant difference between the two groups in the primary endpoint of overall mortality. The group that received rhythm-control therapy, however, exhibited a trend toward increased risk of mortality and ischemic stroke (ischemic stroke occurred mainly in patients who were not receiving adequate anticoagulation).[17] A post-hoc, on-treatment analysis of these data found that patients who were in sinus rhythm had a 47% lower risk of mortality.[18] Of note, however, patients who achieved sinus rhythm with an antiarrhythmic agent did not benefit from this reduced risk because the use of these agents was found to confer a 49% increase in mortality.[18]

The RACE trial enrolled 522 patients (mean age of 68 years) with persistent AF despite previous electrical cardioversion.[19] All patients received anticoagulation and were randomly assigned to either a rate- or rhythm-control strategy. The primary endpoint was a composite of thromboembolic complications, heart failure, death from cardiovascular causes, bleeding, pacemaker implantation, or severe drug-related adverse events. Like the AFFIRM trial, no significant morbidity or mortality advantage was observed with either strategy at the end of the follow-up period.[19]

The results of these studies are most applicable to older patients with comorbid disorders.[2] Although rate control may be the most appropriate and safest initial strategy in older patients, attempts to restore and maintain sinus rhythm should be considered in younger, symptomatic patients who have minimal underlying CVD or in older patients with persistent symptoms despite rate-control therapy. It is likely that a "window of opportunity" exists early in the course of AF to restore sinus rhythm, as long-term AF results in electrical and anatomical remodeling that makes rhythm maintenance increasingly difficult; however, data supporting the benefit of early rhythm control are currently lacking.[2]

Rate Control. The rapid ventricular rate that often accompanies AF should be addressed because it typically causes symptoms, hemodynamic stress, and—if allowed to persist—tachycardia-induced cardiomyopathy.[2] The 2011 ACCF/AHA/HRS Focused Update advises that strict rate control (defined as < 80 beats per minute [bpm] at rest or < 110 bpm during a 6-minute walk) does not offer additional therapeutic benefit over more lenient control (a resting heart rate of < 110 bpm) in patients with persistent AF who have stable ventricular function and minimal or no AF-related symptoms.[12] This recommendation is based on results from the RACE II trial of 614 patients with permanent AF who were randomly assigned to a treatment strategy to achieve either lenient or strict heart-rate control.[20] The primary composite endpoint consisted of death from cardiovascular causes, hospitalization due to heart failure, and stroke, thromboembolism, bleeding, and life-threatening arrhythmias. After 3 years of follow-up, a strategy of lenient heart-rate control was found to be noninferior to a strict heart-rate control strategy with regard to the estimated cumulative incidence of the primary outcome (12.9% vs. 14.9%, respectively; HR, 0.84; 90% CI, 0.58-1.21). It should be noted, however, that at the end of the follow-up period, there was only a 9-bpm difference in the mean resting heart rate of the two groups (strict-control group, 76 bpm ± 14 vs. lenient-control group, 85 bpm ± 14 bpm).[20] Discerning the clinical significance of this difference requires additional research that should be conducted before broad recommendations regarding heart-rate goals in AF are made.

Pharmacologic rate-control agents are effective in approximately 54% to 70% of patients with AF.[21] In persistent or permanent AF, rate control can be achieved with oral beta blockers or non-dihydropyridine calcium channel antagonists.[3] In severely compromised patients, these medications

may be administered intravenously, but caution should be exercised in hypotensive patients and in those with heart failure. Digoxin is no longer considered a first-line agent for rate control in AF, except possibly in patients who are sedentary or who have left ventricular (LV) dysfunction or heart failure; it may be combined with beta blockers or non-dihydropyridine calcium channel antagonists. When first-line medications fail to control rate, intravenous amiodarone or ablation of the AV node or accessory pathways are reasonable alternatives.[3]

Maintenance of Sinus Rhythm. One of the challenges in AF management is deciding whether to pursue long-term maintenance of sinus rhythm in recurrent paroxysmal or persistent AF. Presumed benefits of maintaining sinus rhythm include fewer symptoms, improved exercise tolerance, improved quality of life, and lower risk of stroke.[19] Available antiarrhythmic drugs include the Vaughan-Williams class IC drugs flecainide and propafenone, class III drugs sotalol and dofetilide, and the mixed-action drugs amiodarone and dronedarone.[3] Amiodarone (used off-label for AF) maintains sinus rhythm in approximately 65% of patients, but causes serious extracardiac organ toxicities in 3% to 15% of patients; thus, despite its superior efficacy compared with other agents, it is usually recommended as a second-line agent, except in heart failure.[3,22,23] Other antiarrhythmic agents have an overall efficacy of approximately 35% to 52% and generally lack extracardiac organ toxicity, but some carry a significant risk of proarrhythmias that can be life threatening (Table 2).[3,24,25]

Given the limitations of currently available antiarrhythmic agents and the fact that AF, in the presence of adequate anticoagulation and heart-rate control, is rarely likely to be fatal, guidelines advise that the selection of therapy should be driven primarily by safety considerations rather than efficacy.[3] The 2006 ACC/AHA/ESC guidelines and the 2011 ACCF/

TABLE 2. Guideline-Recommended Drugs in the Maintenance of Sinus Rhythm

DRUG[a]	DAILY DOSAGE	ADVERSE EFFECTS
Amiodarone (Cordarone, Pacerone)[b]	100-400 mg (loading dose of 600 mg/day for 1 month or 1,000 mg/day for 1 week)	GI upset, dermatologic complications, polyneuropathy, pulmonary toxicity, hepatic toxicity, bradycardia, new or worsened arrhythmias, CHF, thyroid dysfunction, eye complications
Dofetilide (Tikosyn)	500-1,000 mcg (requires in-hospital initiation during which dose should be adjusted for renal function and QT-interval response)	Headache, chest pain, dizziness, new or worsened arrhythmias, AV block, bundle branch block, heart block, bradycardia, cardiac arrest, sudden death, angina, HT, syncope
Dronedarone (Multaq)	400 mg, twice daily	GI upset, asthenia, bradycardia, death due to worsening HF, QT prolongation, acute liver failure (rare)
Flecainide (Tambocor)	200-300 mg	GI upset, dizziness, headache, new or worsened arrhythmias in patients with structural heart disease, cardiac arrest, new or worsened CHF, second- or third-degree AV block, bradycardia, sinus pause or arrest, tachycardia, angina, HT, hypotension, visual disturbances
Propafenone (Rythmol, Rythmol SR)	450-900 mg	GI upset, dizziness, headache, new or worsened arrhythmias in patients with structural heart disease, cardiac arrest, first-degree AV block, intraventricular conduction delay, CHF, bradycardia, bundle branch block, atrial flutter, AV dissociation, sick sinus syndrome, sinus pause or arrest, supraventricular tachycardia, prolongation of the PR and QRS intervals
Sotalol (Betapace)	160-320 mg (requires in-hospital initiation during which dose should be adjusted for renal function and QT-interval response; in-hospital initiation may not be necessary for patients who are in sinus rhythm and do not have any risk markers for torsades de pointes)	GI upset, ECG abnormalities, cardiac death, new or worsened CHF, bradycardia, angina, HT, syncope, hypotension, worsening of pulmonary disease

[a]Drugs are listed alphabetically, not in order of suggested use.
[b]Not an FDA-approved indication
AV = atrioventricular; CHF = congestive heart failure; ECG = electrocardiogram; GI = gastrointestinal; HF = heart failure; HT = hypertension
Data derived from National Drug Monograph. Dronedarone (Multaq®). VA Pharmacy Benefits Management Services. January 2010; *ACCF/AHA Pocket Guideline. Management of Patients With Atrial Fibrillation*. American College of Cardiology Foundation and American Heart Association, 2011.

AHA/HRS Focused Update include an algorithm for the selection of a therapeutic strategy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent AF based on the presence of underlying CVD (Figure 1).[3,12]

Roundtable Perspective:
A Safety-Based Approach to Rhythm Control

Gerald V. Naccarelli, MD

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Dronedarone was added as a therapeutic choice for the maintenance of sinus rhythm in patients with recurrent paroxysmal or persistent AF in the 2011 ACCF/AHA/HRS Focused Update.[3,12] This agent was added based on results from the ATHENA trial, which demonstrated a significant reduction in the combined endpoint of cardiovascular hospitalization or death in the dronedarone group versus placebo (31.9% vs. 39.4%, respectively; $P < 0.001$).[26] However, the safety profile of dronedarone continues to evolve, and it is contraindicated in the presence of heart failure. In addition, the PALLAS trial documented an increased risk of stroke and death in patients with permanent AF compared with placebo and was stopped early.[27,28] Accordingly, the FDA announced a labeling change in December 2011 that warns against using dronedarone in patients with permanent AF due to the significant increase in the risk of death or serious cardiovascular events in this population.[29]

Catheter ablation remains a choice of therapy in patients who have failed at least one antiarrhythmic medication.[30] The procedure may offer benefits over pharmacologic strategies; curative catheter ablation to restore sinus rhythm improves quality of life, decreases mortality risk, and has a favorable safety profile.[30] The clinical benefits of catheter ablation compared with antiarrhythmic drug therapy is currently being investigated in the CABANA trial and other studies.

Appropriate patient selection for catheter ablation is critical for success. Guidelines note that catheter ablation yields the best results in patients with symptomatic paroxysmal AF who have failed treatment with one or more antiarrhythmic drugs and who have normal or mildly dilated atria, normal or mildly reduced ventricular function, and no severe pulmonary disease.[12] A new recommendation in the 2011 ACCF/AHA/HRS Focused Update is that catheter ablation may also be a reasonable therapeutic choice to treat symptomatic paroxysmal AF in patients with significant left atrial dilatation or LV dysfunction.[12] However, the highest cure rates can be expected in patients with paroxysmal AF and a structurally normal heart.[30] Major adverse events are reported in approximately 6% of patients and include thromboembolism, pulmonary vein stenosis, left atrial flutter, atrioesophageal fistula, tamponade, pericarditis, and, rarely, death.[3]

Although numerous studies have documented improvements in short-term outcomes of up to 1 year or more, prolonged follow-up to assess the long-term durability and safety of catheter ablation is needed.[3] A recent single-center study of 100 patients (average age of 55.7 years) with AF found that arrhythmia-free survival rates after a single catheter ablation procedure were 40%, 37%, and 29% at 1, 2, and 5 years, respectively.[31] Patients with long-standing persistent AF were almost twice as likely to experience a recurrence compared to those with paroxysmal or persistent AF (HR, 1.9; 95% CI, 1.0-3.5; $P < 0.05$). Valvular heart disease (HR, 6.0; 95% CI, 2.0-17.6; $P = 0.0012$) and nonischemic dilated cardiomyopathy (HR, 34.0; 95% CI, 6.3-182.1; $P < 0.0001$) were independent predictors of recurrence, the majority of which occurred within the first 6 months. Arrhythmia-free survival following the last catheter ablation procedure per patient was 87%, 81%, and 63% at 1, 2, and 5 years, respectively. Although the overall incidence of major complications was low in this study (3%), these results suggest that the efficacy of catheter ablation slowly wanes over time.[31]

Roundtable Perspective:
Catheter Ablation

James A. Reiffel, MD
Oussama M. Wazni, MD

Listen Now

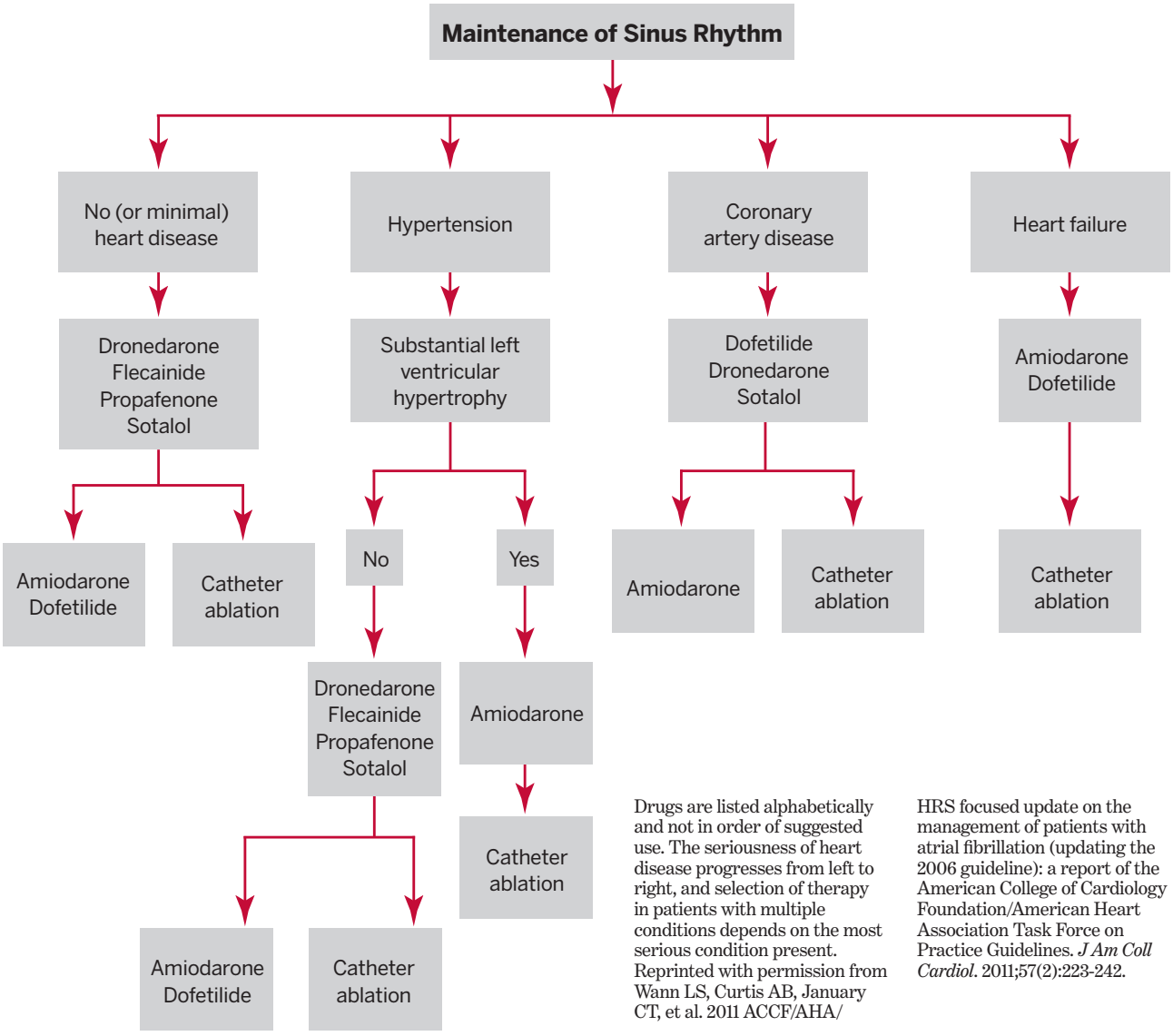
OVERCOMING CHALLENGES IN AF TREATMENT

AF is a complex, chronic condition that is one of the most clinically challenging cardiovascular diseases to manage. Thus, it is no surprise that there are physician- and patient-related barriers to optimal outcomes in AF management. An international quantitative survey of 810 physicians and 825 patients with AF helped to clarify perceptions and attitudes associated with AF.[32] When physicians were asked to rate the most demanding chronic cardiac conditions encountered in clinical practice, only heart failure ranked consistently higher than AF in terms of management difficulty and demands on time. More than 25% of physicians felt that either they lacked time to adequately discuss AF with patients or the condition was too complicated to explain. The majority of patients viewed their physicians as their primary source of AF-related education; however, most physicians reported that patient education materials on AF were inadequate.[32]

The following educational interventions can be employed by clinicians or other office staff to improve communication with patients[33]:

- Present information in a format or manner that is matched to the patient's level of health literacy
- Use a teach-back strategy (eg, ask the patient to explain back to the clinician details about prescribed medications, their benefits, use, and potential side effects)
- Provide patient education materials in a variety of formats, such as pamphlets, instruction sheets, and links to reliable patient education Web sites
- Limit the amount of new information presented at

FIGURE 1. Updated 2011 ACCF/AHA/ESC Algorithm for the Maintenance of Sinus Rhythm in AF



Drugs are listed alphabetically and not in order of suggested use. The seriousness of heart disease progresses from left to right, and selection of therapy in patients with multiple conditions depends on the most serious condition present. Reprinted with permission from Wann LS, Curtis AB, January CT, et al. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2011;57(2):223-242.

Roundtable Perspective: Rhythm-Control Algorithm

Dr. Reiffel: *Selecting for antiarrhythmic therapies, be they ablative or pharmacologic, requires that we consider the particular agent, the particular procedure, and the nature of the patient's heart disease. The class-IC antiarrhythmic drugs are often reasonable first-line choices and virtually devoid of organ-toxic risk. They work about 50% of the time, but they can be proarrhythmic in the setting of certain types of structural heart disease. So while they're suggested as first-line options in minimal heart disease or hypertension with neither left ventricular hypertrophy (LVH) nor ischemia, they're not listed in other circumstances because the proarrhythmic risk then becomes exceedingly high. Sotalol is suggested as a first-line agent. It's not organ toxic, and if used properly and cautiously, its proarrhythmic risk should be no more than about 1%. Although torsades de pointes can be fatal, most cases are not. Conversely, in the setting of LVH or electrolyte disorders, sotalol's proarrhythmic risk increases. So with advanced hypertension, it, too, drops off the list. The same would be true of dofetilide, which has been suggested as a second-line option. It's not organ toxic but has many drug interactions. Its dosing is a little more complex, and in its developmental studies, its incidence of torsades des pointes may have been a little higher. Some of the enthusiasm for dronedarone has waned a bit with some of its trials. It really looks like it belongs where the IC's belong, except it can be used with structural disease in the absence of heart failure. Additionally, it is important to emphasize that one recurrence of AF does not define failure of a therapy. The frequency, duration, and severity of recurrences must all be considered—in the context of the pattern that existed before therapy and with respect to the patient's current quality of life. For example, in a patient with prior frequent paroxysmal AF and occasional persistent AF, a pattern on therapy of infrequent short paroxysmal AF may well be determined to be effective therapy.*

Roundtable Perspective:
Improving Patient-Clinician Communication and Patient Adherence

Dr. Reiffel: *Patient education is the key. If you get patients to understand what their disorder is, what their prognosis is, what they can do to help it, and what the future will be like, you've got a better chance of successful therapy. I will rarely put patients on antiarrhythmic therapy or talk about ablation after the first or second episode. I want to get a sense of how often they're having episodes and how severe those episodes are. Also, if patients understand that recurrences will continue in the absence of therapy, they are more apt to cooperate with the therapy employed.*

Dr. Naccarelli: *Communication is important. It can be useful to point out some things that could help them, such as a medication log to keep their prescriptions straight, online educational material on AF or ablation, patient-education handouts, or office-based resources like their doctor and other available staff (eg, nurse practitioners or PAs).*

Dr. Wazni: *A lot of times I find that patients are really very worried about AF, so I try to reassure them in the beginning. I explain that once you take care of anticoagulation and rate control, then AF should not be a deadly disease. I review with them the three foundations of AF treatment: anticoagulation, rate control, and symptom relief. We try to simplify medications as much as we can.*

each visit to avoid overwhelming the patient
- Make use of tools that can facilitate patient-physician communication such as the medication log included with this publication (see Appendix)

Medication adherence is a common problem in the management of any chronic disease, and AF is no exception.[33] Physician barriers include a lack of time for medication counseling and poor communication with patients. Patient barriers may be related to poor health literacy, personal or cultural beliefs about their condition or medications, advanced age or dementia, and difficulty coping with multiple comorbidities. Additionally, cost-related barriers, complex medication regimens, and adverse effects contribute to this issue.[33]

Complex medication regimens are common in patients with CVD. A recent study of a large cohort of individuals filling prescriptions for a statin or an angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) assessed the association of therapeutic complexity to poor medication adherence.[34] Prescription claims data from more than 2.5 million CVD patients were examined over a 3-month period. Participants filled an average of 6 different drug classes prescribed by an average of 2 clinicians. Mean medication adherence in the statin and ACEI/ARB cohorts was 68.6% and 66.4%, respectively. After controlling for demographics, comorbidity, and copayments, independent predictors of worse medication adherence included a greater number of prescribers, visits to more pharmacies, and less refill consolidation to a single pharmacy home. In the ACEI/ARB group, adherence fell by 2.4% for each additional daily medication dosage.[34]

Physicians play a key role in maximizing medication adherence and should consider implementing the following strategies to improve adherence[33]:

- Simplify the regimen and provide clear instructions
- Customize the regimen to fit the patient's clinical situation and lifestyle by considering goals of treatment, prognosis, the patient's cognitive abilities, and social support system
- Provide simple adherence tools, such as medication organizers or charts (see Appendix), reminder calls, or e-mails
- Suggest behavioral strategies to simplify medication dosing, such as linking medication use with daily habits (eating meals, brushing teeth, etc.)
- Have office staff follow up by phone within a few days of an appointment

Roundtable Perspective:
Adherence Tools

Gerald V. Naccarelli, MD
James A. Reiffel, MD

Listen Now

CONCLUSION

The primary goals in the management of AF are preventing stroke and early death, minimizing symptoms, and improving quality of life. However, patients with AF have individual management needs depending on risk of thromboembolism, the severity of symptoms, their age, the presence of comorbidities, and other factors. Clinical decision making regarding rate- and rhythm-control strategies must take these factors into consideration to arrive at the most appropriate approach for each patient. Additionally, ensuring optimal therapeutic outcomes requires the identification and management of barriers to successful patient-clinician communication and medication adherence.

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WEEK_____

Patient name: _____ Physician name: _____

Week start date: _____

MEDICATION INFORMATION					DATE TAKEN						
	MEDICATION	DOSE	FREQUENCY	TIME TAKEN							
1				DOSE 1 TIME							
				DOSE 2 TIME							
				DOSE 3 TIME							
2				DOSE 1 TIME							
				DOSE 2 TIME							
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3				DOSE 1 TIME							
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NOTES: _____

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IMPROVING QUALITY OF LIFE IN PATIENTS WITH ATRIAL FIBRILLATION THROUGH SAFER, MORE INDIVIDUALIZED TREATMENT APPROACHES

CME EVALUATION AND POST-SURVEY

Release Date: August 21, 2012 Expiration Date: August 20, 2013

SA179CAR12 NL1 8-21-12 1/3

To submit for credit, complete this evaluation and attestation. If completing the print version below, please use all capital letters and print your name, address, and other information requested below. Keep a copy of the completed evaluation, surveys, and post-test for your records and mail originals to Med-IQ, 5523 Research Park Drive, Suite 210, Baltimore, Maryland, 21228, or fax to 443 543 5210 by August 20, 2013; certificates will be mailed 4 to 6 weeks after receipt. To complete the evaluation online, please visit www.Med-IQ.com/a666; certificates can be printed immediately.

The purpose of this evaluation is to receive your feedback so we may improve future educational activities. All responses are confidential but may be evaluated in aggregate.

PARTICIPANT INFORMATION

Date of Participation in Activity: _____

First Name: _____ Last Name: _____

Degree/Profession: ❒ MD ❒ DO ❒ PharmD ❒ RPh ❒ PhD ❒ PA ❒ RN ❒ NP ❒ LPN ❒ Other: _____

Specialty: ❒ Electrophysiology ❒ Cardiology ❒ Family Practice ❒ General Practice ❒ Internal Medicine ❒ Other: _____

Address 1: _____

Address 2: _____

City/State/Zip: _____

Phone: _____ Fax: _____ E-mail: _____

Type of practice: ❒ Community/Private ❒ Academic ❒ Hospital ❒ HMO ❒ Other: _____

Approximately how many patients do you see each week? _____

Approximately what percentage of the patients you see each week have atrial fibrillation? _____ %

ACTIVITY EVALUATION

Rate the extent to which this CME activity met the following learning objectives:	Minimally 1	2	3	4	5	6	Completely 7	N/A
1. Describe the potential contribution of patient factors and adherence on the progression of AF and disease-related outcomes, and employ strategies to address these factors	❒	❒	❒	❒	❒	❒	❒	❒
2. Identify available pharmacologic treatment options for rate and rhythm control in patients with AF, and discuss how their respective safety and efficacy profiles factor into the development of individualized care plans	❒	❒	❒	❒	❒	❒	❒	❒
3. Assess current evidence regarding appropriate candidates, short- and long-term efficacy and safety, and optimal sequencing of catheter ablation for the management of AF	❒	❒	❒	❒	❒	❒	❒	❒

Rate the extent to which this CME activity:	Minimally 1	2	3	4	5	6	Completely 7	N/A
Met your expectations	❒	❒	❒	❒	❒	❒	❒	❒
Is applicable to your practice	❒	❒	❒	❒	❒	❒	❒	❒
Used appropriate teaching methods	❒	❒	❒	❒	❒	❒	❒	❒
Provided current scientific evidence to support content	❒	❒	❒	❒	❒	❒	❒	❒
Addressed barriers to optimal patient management	❒	❒	❒	❒	❒	❒	❒	❒
Provided useful non-educational resources (eg, patient handouts, tools to assess practice, resources)	❒	❒	❒	❒	❒	❒	❒	❒
Addressed the following 6 core competencies:								
Patient care	❒	❒	❒	❒	❒	❒	❒	❒
Medical knowledge	❒	❒	❒	❒	❒	❒	❒	❒
Interpersonal and communication skills	❒	❒	❒	❒	❒	❒	❒	❒
Professionalism	❒	❒	❒	❒	❒	❒	❒	❒
Systems-based practice	❒	❒	❒	❒	❒	❒	❒	❒
Practice-based learning and improvement	❒	❒	❒	❒	❒	❒	❒	❒

Compared to all other CME activities similar to this one that I have participated in over the past year, I would rate this program as:	Needs Improvement 1	2	3	Average 4	5	Outstanding 6	7
	❒	❒	❒	❒	❒	❒	❒

Did this activity provide fair and balanced content free from commercial bias? ❒ Yes ❒ No

(Commercial bias is defined as information presented that advocates a specific proprietary business product or service of a commercial interest.)

If no, please explain: _____

As a result of this learning experience, what will you do differently in the care of your patients? _____

_____

How will you implement these changes? _____

Which of the following practice changes do you intend to implement as a result of participating in this learning experience?

A. I will identify patients with risk factors for AF progression and proactively manage these factors

B. I will account for symptom burden and other patient-related factors (eg, age, comorbidities) when designing individualized treatment strategies for my patients with AF

C. I will consider invasive AF management strategies for symptomatic AF patients as appropriate

D. I will routinely inquire about patients' medication-taking behaviors and integrate simple tools to help improve medication adherence into my practice

E. Other (please specify): _____

F. None

Are there specific barriers to the management of patients with atrial fibrillation that you feel better equipped to address as a result of this activity? If so, please list them. _____

Are there specific barriers to the management of patients with atrial fibrillation that this activity did not address? If so, please list them.

_____

I would like to see CME activities on these topics: _____

Other comments (eg, what can we do to improve future CME activities?): _____

ATTESTATION AND SIGNATURE REQUIRED TO RECEIVE CREDIT AND CREDIT REDEMPTION:

Physicians: I claim ❒ _____ (maximum 1.0) *AMA PRA Category 1 Credit™*

Signature: _____ **Date:** _____

NURSES: must provide license # to redeem credit _____

Name

(Please Print)

Post-Survey/Post-Test

Please take a moment to complete the following questions by circling the optimal answer. Participants seeking credit for this activity will be graded ONLY on the four questions enclosed in the box below; at least 70% of these questions must be answered correctly. The other questions on this page will NOT be graded; they are collected for informational purposes only to help us assess the effectiveness of this educational activity. If you are redeeming credit for this activity online, you will be prompted to answer these questions in our online system after clicking the "Get Credit" button.

1. How confident are you in your ability to select the most appropriate guideline-recommended therapy for your patients with AF?

A. Extremely confident
B. Moderately confident
C. Somewhat confident
D. Not confident at all

2. How confident are you in your ability to determine whether a patient with AF is an appropriate candidate for catheter ablation?

A. Extremely confident
B. Moderately confident
C. Somewhat confident
D. Not confident at all

3. How likely are you to provide the medication log presented in this activity to your patients with AF as a method to improve their medication adherence?

A. Extremely likely
B. Moderately likely
C. Somewhat likely
D. Not likely at all

4. Based on the HATCH score, which of the following patients with paroxysmal AF would be most likely to progress to persistent or permanent AF?

A. A 68-year-old man with a history of stroke and heart failure
B. A 70-year-old man with hypertension and heart failure
C. A 73-year-old man with COPD and a history of stroke
D. A 76-year-old man with hypertension and COPD
E. I am unfamiliar with the HATCH score

5. Guidelines advise that the selection of an antiarrhythmic agent for patients with AF should primarily be driven by:

A. Efficacy
B. Safety
C. Patient preference
D. Tolerability of side effects

6. Which of the following statements about catheter ablation is TRUE?

A. The highest cure rates can be expected in patients with paroxysmal AF and a structurally normal heart
B. Treatment-naïve patients with recently diagnosed AF are optimal candidates
C. It should not be considered as an option for patients with symptomatic paroxysmal AF who have LV dysfunction
D. Longer-term follow-up studies suggest that more than 30% of patients remain arrhythmia free after a single procedure at 5 years

7. In the Euro Heart Survey, what percentage of patients with paroxysmal AF and a baseline HATCH score of > 5 progressed to more sustained forms of AF at a 1-year follow-up?

A. 15%
B. 25%
C. 50%
D. 75%

8. According to AHA/ASA and ACCP/AHA/HRS updated guidelines, which of the following agents is NOT currently recommended for anticoagulation in a patient with AF and 1 moderate-risk factor?

A. Aspirin
B. Dabigatran
C. Rivaroxaban
D. Warfarin

9. Updated guidelines for rate control in AF recommend that rate control to < 80 bpm at rest or < 110 bpm during a 6-minute walk is more beneficial than rate control to < 110 bpm at rest.

A. True
B. False

10. According to the 2011 ACCF/AHA/HRS Focused Update, which of the following agents would be a first-line choice for the maintenance of sinus rhythm in a patient with persistent AF and coronary artery disease?

A. Amiodarone
B. Dronedarone
C. Propafenone
D. Any of the above

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