

Medical Insiders™
Complimentary CME

Current Practices in AF Management: **Are Guideline-Based Options Driving Better Outcomes?**

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Activity Overview

This 30-minute *Medical Insiders* accredited CME webcast features expert cardiologists Gerald V. Naccarelli, MD, and James A. Reiffel, MD, and electrophysiologist E. Magnus Ohman, MD, FRCPI, FESC, FACC, FSCAI. These faculty provide insight on specific challenges clinicians face when managing patients with atrial fibrillation (AF) and discuss best practices in developing individualized treatment plans to prevent AF progression, reduce hospitalizations, and decrease the risks of morbidity and mortality.

Target Audience

This activity is intended for cardiologists and electrophysiologists.

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Faculty

Gerald V. Naccarelli, MD

Bernard Trabin Chair in Cardiology
Professor of Medicine
Chief, Division of Cardiology
Pennsylvania State University College of Medicine
The Milton S. Hershey Medical Center
Hershey, PA

James A. Reiffel, MD

Professor (Emeritus) of Medicine and Special Lecturer
Columbia University Vagelos College of Physicians and Surgeons
Department of Medicine, Division of Cardiology,
Electrophysiology Section
New York, NY

E. Magnus Ohman, MD, FRCPI, FESC, FACC, FSCAI

Professor of Medicine
The Kent and Siri Rawson Director, Duke Program for
Advanced Coronary Disease
Vice-Chair, Department of Medicine - Development and
Innovation
Associate Director, Duke Heart Center
Senior Investigator, Duke Clinical Research Institute
Duke University Medical Center
Durham, NC

Activity Planners

Iwona Misiuta, PhD, MHA
Clinical Content Manager
Med-IQ
Baltimore, MD

Samantha Gordon
CME Specialist
Med-IQ
Baltimore, MD

Kathryn Schaefer, MSN, RN, CPHRM
Senior Manager, Accreditation and Compliance
Med-IQ
East Lansing, MI

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Faculty Disclosure Statements

Gerald V. Naccarelli, MD

Consulting fees/advisory boards: Ascension, OMEICOS Therapeutics, Janssen Pharmaceuticals, Inc., Milestone Pharmaceuticals, Inc.

Contracted research: Janssen Pharmaceuticals, Inc.

E. Magnus Ohman, MD, FRCPI, FESC, FACC, FSCAI

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James A. Reiffel, MD

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Learning Objectives

Upon completion, participants should be able to:

- Identify criteria and tools to facilitate the assessment of ongoing AF symptoms and patients' quality of life
- Select appropriate individualized treatments for patients with AF based on disease- and patient-related factors

AF: A Significant Healthcare Issue in the US

- Affects an estimated 2.7-6.1 million people¹
 - ~2% of people < 65 years old¹
 - ~9% of people ≥ 65 years old¹
- Causes more than 750,000 hospitalizations each year¹
 - Contributes to an estimated 130,000 deaths each year
- Costs an estimated \$6 billion each year¹
- Is underestimated due to lack of symptoms (silent AF)²
 - ~45% of SPAF-III trial participants had AF detected incidentally

1. CDC. www.cdc.gov/dhdsr/data_statistics/fact_sheets/fs_atrial_fibrillation.htm;
2. Turakhia MP, et al. *PLoS One*. 2018;13:e0195088.

What Are the Goals of AF Therapy?

- Improve survival
- Reduce sequelae
 - Stroke
- Reduce hospitalizations
- Improve symptoms
- Improve QOL, **which encompasses all of the above**
- Restore atrial function/reverse the remodeling process—AF begets AF; sinus rhythm begets sinus rhythm and helps reverse electrical, histologic, and anatomic remodeling

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AF Therapies: Multiple Options and Interventions

- Ventricular rate control
 - Pharmacologic or rarely AV node ablation and pacing
- Rhythm control
 - AAD and/or ablative procedures
- Thromboembolism prevention
 - Usually OACs; infrequently device or surgical approaches to the LAA

- The key is to individualize therapy to maximize benefit and minimize risk for each patient

Trials of Rhythm and Rate Control in AF: AFFIRM, RACE, AF-CHF, PIAF, STAF, HOT CAFÉ

- Major overall findings¹⁻⁹
 - Rhythm control was not superior to rate control in terms of morbidity/mortality
 - Rate control is an acceptable primary therapeutic option
 - Patients with AF and risk factors for stroke should receive anticoagulation indefinitely, even when sinus rhythm appears to be restored and maintained
- Both strategies are acceptable primary therapeutic options, but...

1. Ogawa S, et al. *Circ J*. 2009;73:242-8; 2. Roy D, et al. *N Engl J Med*. 2008;358:2667-77; 3. Reiffel JA. *J Atr Fibrillation*. 2008;1:21; 4. Opolski G, et al. *Chest*. 2004;126:476-86; 5. Vora A, et al. *J Cardiovasc Pharmacol Ther*. 2004;9:65-73; 6. Carlsson J, et al. *J Am Coll Cardiol*. 2003;41:1690-6; 7. Wyse DG, et al. *N Engl J Med*. 2002;347:1825-33; 8. Van Gelder IC, et al. *N Engl J Med*. 2002;347:1834-40; 9. Hohnloser SH, et al. *Lancet*. 2000;356:1789-94.

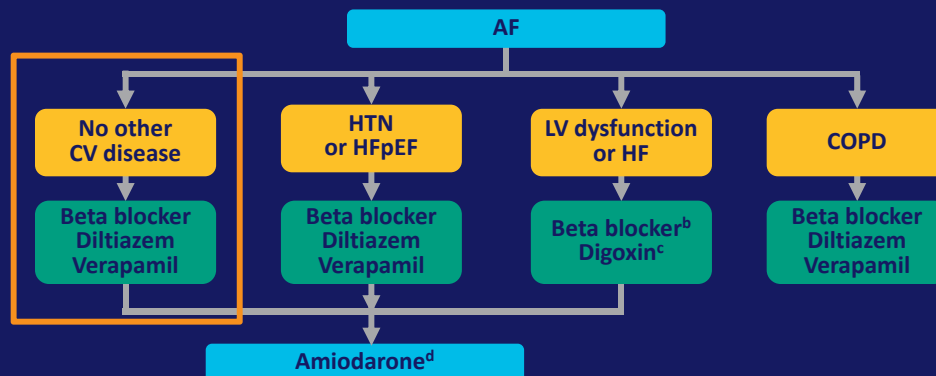
Trials of Rhythm and Rate Control in AF (cont'd):

AFFIRM, RACE, AF-CHF, PIAF, STAF, HOT CAFÉ

- Rate control is not appropriate for all patients with AF¹
 - Particularly very symptomatic patients (symptomatic despite rate control)²
 - Young patients³
 - Patients in whom exercise tolerance is important⁴
 - Patients in whom rate control failed⁴
 - Some patients with depressed LV function³
- Clinicians should adapt the therapeutic strategy to the individual

1. Reiffel JA. *J Atr Fibrillation*. 2008;1:21; 2. Ogawa S, et al. *Circ J*. 2009;73:242-8;
3. Wyse DG, et al. *N Engl J Med*. 2002;347:1825-33; 4. Vora A, et al. *J Cardiovasc Pharmacol Ther*. 2004;9:65-73.

AHA/ACC/HRS: AF Rate Control^a



^aSee package insert for full prescribing information and adverse events.

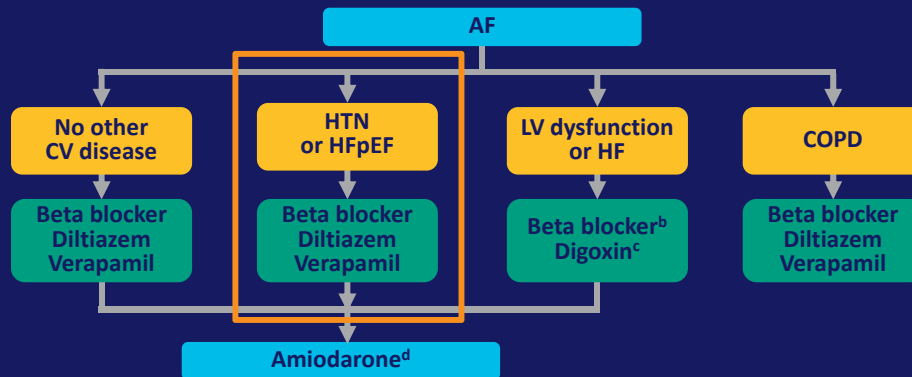
^bBeta blockers should be instituted following stabilization of patients with decompensated HF. The choice of beta blocker (eg, cardioselective) depends on the patient's clinical condition.

^cDigoxin is not usually first-line therapy. It may be combined with a beta blocker and/or a nondihydropyridine calcium channel blocker when ventricular rate control is insufficient and may be useful in patients with HF.

^dIn part because of concern over its side-effect profile, use of amiodarone for chronic control of ventricular rate should be reserved for patients who do not respond to or are intolerant of beta blockers or nondihydropyridine calcium antagonists.

January CT, et al. *J Am Coll Cardiol*. 2014;64:e1-76.

AHA/ACC/HRS: AF Rate Control^a



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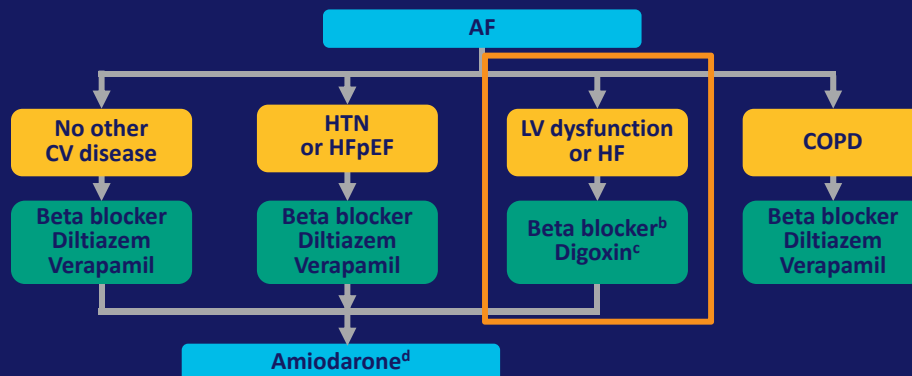
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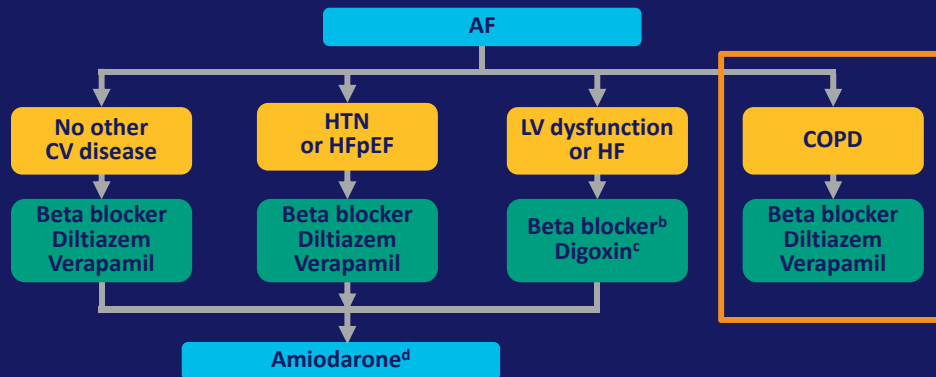
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January CT, et al. *J Am Coll Cardiol*. 2014;64:e1-76.

AHA/ACC/HRS: AF Rate Control^a



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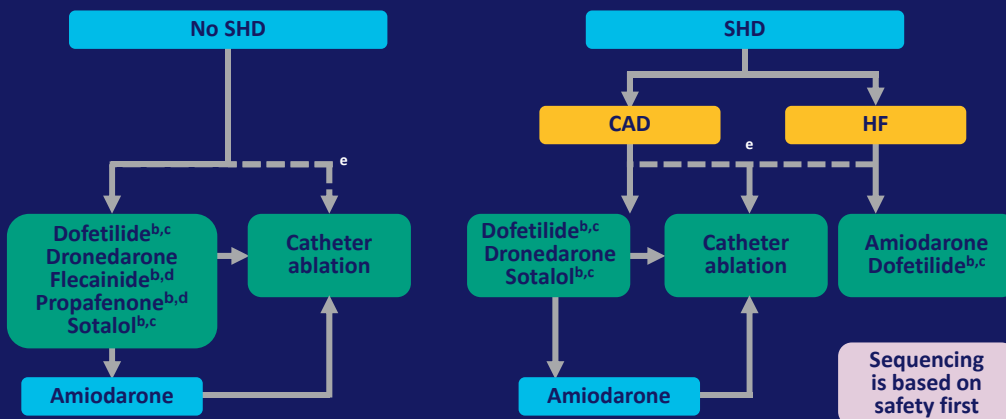
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January CT, et al. *J Am Coll Cardiol*. 2014;64:e1-76.

AHA/ACC/HRS: AF Rhythm Control^a



^aSee package insert for full prescribing information and adverse events.

^bNot recommended with severe LVH (wall thickness > 1.5 cm).

^cShould be used with caution in patients at risk of torsades de pointes ventricular tachycardia.

^dShould be combined with AV nodal blocking agents.

^eDepending on patient preference when performed in experienced centers.

January CT, et al. *Circulation*. 2014;130:2071-104.

AF: Rate vs Rhythm Control

Rate control patient profile

- Asymptomatic AF
- > 65 years old
- Recurrent AF
- History of cardioversion
- Intolerant to AAD
- Patient preference

Current guidelines:

- Pharmacologic therapy can help maintain sinus rhythm in patients with AF

Experts often recommend:

- Attempting rhythm control in most patients
- Applying early intervention to prevent new-onset AF progression to permanent AF

January CT, et al. *Circulation*. 2019;140:e125-51; January CT, et al. *J Am Coll Cardiol*. 2014;64:e1-76; Chen ST, et al. *Prog Cardiovasc Dis*. 2018;60:514-23; Mezue K, et al. *Curr Cardiol Rev*. 2017;13:41-6; Fuster V, et al. *J Am Coll Cardiol*. 2011;57:e101-98; Fuster V, et al. *Circulation*. 2006;114:e257-354.

Antiarrhythmic Therapy With AADs

- AF is usually recurrent, and rarely lethal, so remember to keep the goals realistic:
 - Reduce the frequency, duration, and severity of events
 - Minimize the risks of treatment (eg, drug, ablation)
- AAD therapy (per guidelines) must be selected based not only on anticipated efficacy (most have 40%-60% efficacy), but also on:
 - Safety and long-term tolerance
 - Presence or absence of SHD
 - Proarrhythmic risk and ability to initiate as an outpatient
 - Effects on sinus node and conduction system
 - LV function
 - Drug interaction potential

January CT, et al. *Circulation*. 2019;140:e125-51; Chen ST, et al. *Prog Cardiovasc Dis*. 2018;60:514-23; Mezue K, et al. *Curr Cardiol Rev*. 2017;13:41-6; Fuster V, et al. *J Am Coll Cardiol*. 2011;57:e101-98; Camm AJ, et al. *Eur Heart J*. 2010;31:2369-429; Fuster V, et al. *J Am Coll Cardiol*. 2006;48:e149-246.

Efficacy of Catheter Ablation in Patients With AF

- Efficacy rates depend on:
 - Expertise of physician (expert hands)¹
 - Type of AF being treated (eg, paroxysmal AF, long-standing persistent AF)²
- RFA studies report higher efficacy rates vs AAD therapy and a lower rate of complications^{3,4}
- RFA as first-line therapy in select patients who understand the benefits and risks of the procedure³

Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation The CABANA Randomized Clinical Trial

Douglas L. Packer, MD, Daniel B. Mark, MD, MPH, Richard A. Robb, PhD, Kristi H. Monahan, RN, Tristram D. Bahnson, MD, Jeanne E. Poole, MD, Peter A. Noseworthy, MD, Yves D. Rosenberg, MD, MPH, Neal Jeffries, PhD, L. Brent Mitchell, MD, Greg C. Flaker, MD, Evgeny Pokushalov, MD, Alexander Romanov, MD, T. Jared Bunch, MD, Georg Noeller, MD, Andrey Ardashov, MD, Amirian Revishvili, MD, David J. Wilber, MD, Riccardo Cappato, MD, Karl-Heinz Kuck, MD, Gerhard Hindricks, MD, D. Wyn Davies, MD, Peter R. Kowey, MD, Gerald V. Naccarelli, MD, James A. Reffel, MD, Jonathan P. Piccini, MD, MHS, Adam P. Silverstein, MS, Hussein R. Al-Khalidi, PhD, Kerry L. Lee, PhD, for the CABANA Investigators

1. Packer DL, et al. *JAMA*. 2019;321:1261-74; 2. Mark DB, et al. *JAMA*. 2019;321:1275-85; 3. Hakalahti A, et al. *Europace*. 2015;17:370-8; 4. Chen HS, et al. *Cochrane Database System Rev*. 2012;4:CD007101.

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline^a

- For patients with AF and a CHA₂DS₂-VASc score of ≥ 2 in men or ≥ 3 in women, OACs are recommended
 - Options include warfarin (LOE: A); apixaban (LOE: B); dabigatran (LOE: B); edoxaban (LOE: B-R), or rivaroxaban (LOE: B)
- In patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve), the CHA₂DS₂-VASc score is recommended for stroke risk assessment
- For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) who are unable to maintain a therapeutic INR level with warfarin, use of a NOAC is recommended
- In patients with AF and an increased risk of stroke (based on CHA₂DS₂-VASc risk score of ≥ 2) who have undergone PCI with stenting for ACS, double therapy with a P2Y₁₂ inhibitor (clopidogrel or ticagrelor^b) and dose-adjusted vitamin K antagonist is reasonable to reduce the risk of bleeding as compared with triple therapy
- In patients with AF and an increased risk of stroke (based on CHA₂DS₂-VASc risk score of ≥ 2) who have undergone PCI with stenting for ACS, double therapy with a P2Y₁₂ inhibitor (clopidogrel) and low-dose rivaroxaban 15 mg/day is reasonable to reduce the risk of bleeding as compared with triple therapy

^aSee package insert for full prescribing information and adverse events.

^bOff-label.

January CT, et al. *Circulation*. 2019;140:e125-51; January CT, et al. *J Am Coll Cardiol*. 2014;64:e1-76.

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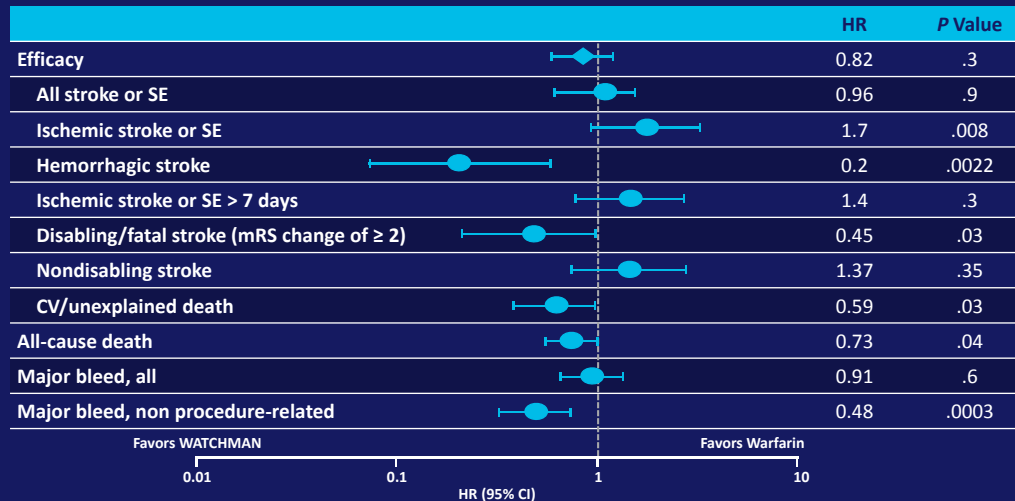
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Device Detection of AF and Atrial Flutter (New)

Recommendations for Device Detection of AF and Atrial Flutter

COR	LOE	Recommendations
I	B-NR	In patients with cardiac implantable electronic devices (pacemakers or implanted cardioverter-defibrillators), the presence of recorded atrial high-rate episodes should prompt further evaluation to document clinically relevant AF to guide treatment decisions
IIa	B-R	In patients with cryptogenic stroke (ie, stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize the detection of silent AF

WATCHMAN LAA Closure Device: 5-Year Meta-Analysis of PROTECT AF, PREVAIL



Reddy VV, et al. *J Am Coll Cardiol*. 2017;70:2964-75.

WATCHMAN: Indications

- The WATCHMAN device is indicated to reduce the risk of thromboembolism from the LAA in patients with nonvalvular AF who:
 - Have an increased risk of stroke and SE based on CHADS₂ or CHA₂DS₂-VASc scores and are recommended for anticoagulation therapy
 - Are deemed by their physicians to be unsuitable for warfarin or DOAC therapy
 - Have an appropriate rationale to seek a nonpharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared with warfarin

Akinapelli A, et al. *Curr Cardiol Rev*. 2015;11:334-40.

Subclinical (Sometimes Called “Silent”) AF

- AF may occur without symptoms
- Subclinical AF can be detected with screening methods
 - The most effective method uses inserted monitors
- In patients with demographic and/or laboratory high-risk markers for both AF and thromboembolism, the value of screening should be highest, as AF detected in such patients may make them appropriate candidates for anticoagulation
 - In such patients, AF incidences near 30% by 12-18 months and up to 40% by 30 months have been reported
 - At least 3 ongoing trials are addressing the issue of anticoagulation in such patients

January CT, et al. *Circulation*. 2019;140:e125-51; Kirschhof P, et al. *Am Heart J* 2017;190:12-18; Reiffel JA, et al. *JAMA Cardiol* 2017;2(10):1120-27.

Patient 1: Julie, 77-Year-Old Woman

History

- 5-year history of permanent AF (average rate on Holter: 78 bpm), known mild AS with a bicuspid valve, and HTN controlled on metoprolol succinate 50 mg/day
- Cr = 1.8 mg/dL
- CrCl = 38 mL/min
- Has been on warfarin (5 mg/day) without bleeding or embolic issues
- TTR = 38%

**Would you make any changes?
How would you assess QOL?**

Patient 2: George, 78-Year-Old Man

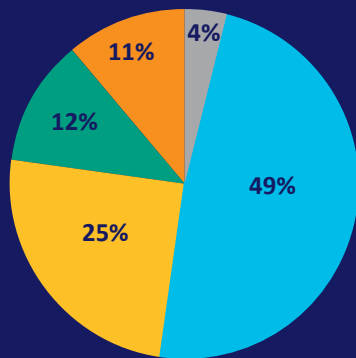
History

- 3-year history of symptomatic paroxysmal AF (5 times a year lasting hours), now controlled with dronedarone 400 mg BID with meals with sinus rate of 68 bpm
- Has HTN, which is treated with diltiazem HCl 240 mg/day, and diabetes, which is treated with metformin 100 mg BID
- 3 months ago, he had a drug-eluting stent inserted in his mid-left anterior descending artery because of a 90% occlusion found at catheterization after he complained of exertional angina
- Additional current medications: atorvastatin 40 mg/day, aspirin 81 mg/day, and clopidogrel 75 mg/day
- CrCl = 66 mL/min

**Would you make any changes?
How would you assess QOL?**

Discussion: Results From Current Practice Questionnaire

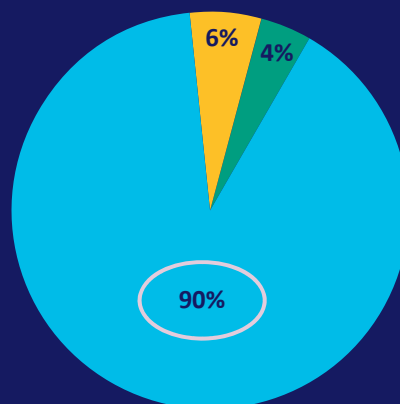
In your practice, which of the following is the greatest barrier to the management of AF?



- Adverse effects of medications
- Patient's lack of understanding about the condition/situation
- Insurance issues
- Lack of adequate time during clinical visit to address AF symptoms and other related health concerns
- Other

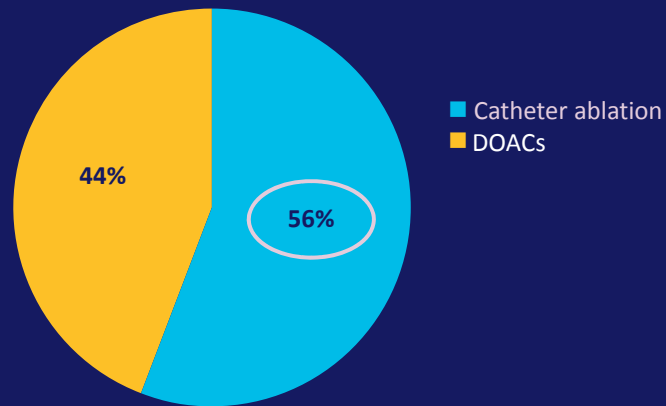
Other:	Count
Inadequate medical efficiency	1
Patient adherence to therapy/lifestyle modification	1
Totals	2

Which of the following is the most effective management strategy to reduce morbidity and mortality in AF?

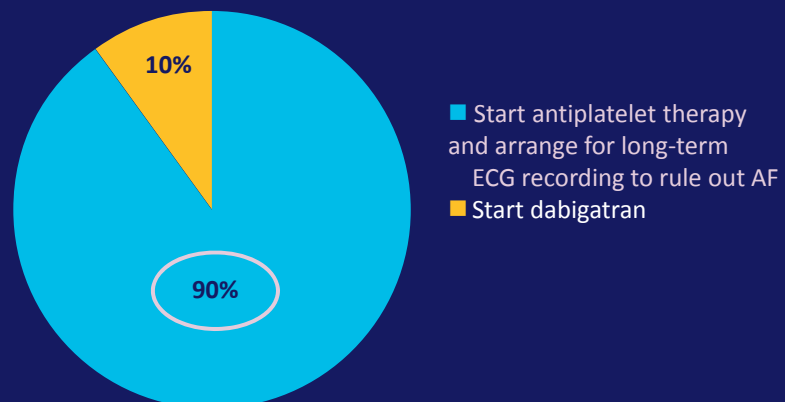


- Anticoagulation
- Rhythm control
- Rate control

Which of the following has been shown to improve mortality rates in patients with symptomatic AF and HF with reduced LV ejection fraction?



AJ, a 55-year-old woman with no prior cardiac history, is admitted with an ischemic stroke of undetermined source. Her ECG, echocardiogram, and in-house telemetry results are normal. Which of the following would you recommend for this patient?



Instructions to Receive Credit

To receive credit, read the introductory CME material, listen to the webcast, and complete the evaluation, attestation, and post-test, answering at least 70% of the post-test questions correctly.

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Call (toll-free) 866 858 7434

Email info@med-iq.com

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Abbreviations and Acronyms

AAD = antiarrhythmic drug

ACC = American College of Cardiology

ACS = acute coronary syndromes

AF = atrial fibrillation

AHA = American Heart Association

AS = aortic stenosis

BID = twice daily

bpm = beats per minute

CAD = coronary artery disease

CBC = complete blood count

CHA₂DS₂-VASc = congestive heart failure, hypertension, age \geq 75 years (2 points), diabetes mellitus, stroke/TIA (2 points), vascular disease, age 65-74 years, sex category

CHADS₂ = congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, and stroke/TIA (2 points)

COPD = chronic obstructive pulmonary disease

Cr = creatinine

CrCl = creatinine clearance

CV = cardiovascular

DOAC = direct-acting oral anticoagulant

ECG = electrocardiogram

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

HRS = Heart Rhythm Society

HTN = hypertension

INR = international normalized ratio

LAA = left atrial appendage

LV = left ventricular

mRS = modified Rankin Scale

NOAC = non-vitamin K oral anticoagulant

NSR = normal sinus rhythm

OAC = oral anticoagulant

PCI = percutaneous coronary intervention

QOL = quality of life

RFA = radiofrequency ablation

SE = systemic embolism

SHD = structural heart disease

TSH = thyroid-stimulating hormone

TTR = time in therapeutic range

SPAF = Stroke Prevention in Atrial Fibrillation