MARCH 2017
VOL. 17, ISSUE 2

IU Health Physicians

ADVANCED praxis CME

A JOURNAL OF CURRENT TRENDS IN MEDICINE FROM IU HEALTH PHYSICIANS, A PARTNERSHIP OF IU SCHOOL OF MEDICINE AND INDIANA UNIVERSITY HEALTH

CASE MANAGEMENT Atrial Fibrillation

ACCREDITATION STATEMENT
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Indiana University School of Medicine (IUSM) and IU Health Physicians. IUSM is accredited by the ACCME to provide continuing medical education for physicians.

DESIGNATION STATEMENT
IUSM designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

FACULTY DISCLOSURE STATEMENT
In accordance with the ACCME Standards for Commercial Support, educational programs sponsored by IUSM must demonstrate balance, independence, objectivity, and scientific rigor. All faculty, authors, editors, and planning committee members participating in an IUSM-sponsored activity are required to disclose any **relevant financial interest or other relationship** with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services that are discussed in an educational activity.

Dr. Gopi Dandamudi has disclosed that he received consulting fees for educational events and clinical research from Medtronic. Any potential conflict of interest has been resolved.

OBJECTIVES
After reading this article, the reader should be able to:

- Summarize the epidemiology, risk factors, and etiology of atrial fibrillation (AF).
- Identify the various possible presentations of AF.
- Describe the three principal goals of AF therapy.
- Discuss the two treatment modalities for the management of AF.
- Assess the available ablation strategies used to improve outcomes for patients with AF.

Date of original release: March 2017
Date of expiration: March 2018

COMMERCIAL SUPPORT
This CME activity does not have any commercial support.

A 58-year-old white female is referred to Indiana University Health Methodist Hospital Atrial Fibrillation Center because of worsening paroxysmal atrial fibrillation (PAF) that has become refractory to antiarrhythmic drug (AAD) therapy with dronedarone or flecainide. She reports increasingly frequent (almost daily) PAF episodes that leave her short of breath and fatigued. She denies any chest pain, orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, syncope, or near-syncope. Her medical history includes non-Hodgkins lymphoma and breast cancer treated with surgical resection and chemotherapy that is in remission. Current medications are apixaban, metoprolol, and flecainide.

Overview of AF

AF is the most common sustained cardiac arrhythmia, affecting an estimated 2.7 to 6.1 million people in the United States, or approximately two percent of individuals <65 years and nine percent of those ≥65 years.[1] Aside from increasing age and family history, hypertension is the greatest risk factor for AF, accounting for more than one-fifth of all cases *(Figure 1)*.[2]

Frequently initiated by rapid firing (triggers) from the pulmonary veins, AF is characterized by uncoordinated atrial activation. Early in the course of the disease, the atrium is relatively healthy, allowing spontaneous restoration of sinus rhythm following arrhythmias occurring with paroxysms. As the substrate remodels over time, mechanical function deteriorates, arrhythmias become persistent, and maintaining or restoring sinus rhythm becomes progressively more difficult.

"AF may present as *paroxysmal*, defined as episodes that terminate spontaneously or with intervention within seven days of onset and may recur with variable frequency; persistent, episodes lasting longer than seven days; or *long-standing persistent*, which implies continuous atrial fibrillation for 12 months or longer,"[3] describes Gopi Dandamudi, MD, assistant professor of medicine at Indiana University School of Medicine and electrophysiologist and director of the IU Health Methodist Atrial Fibrillation Center. "The term *permanent AF* is applied when the patient and physician agree not to pursue strategies to restore and/or maintain sinus rhythm."

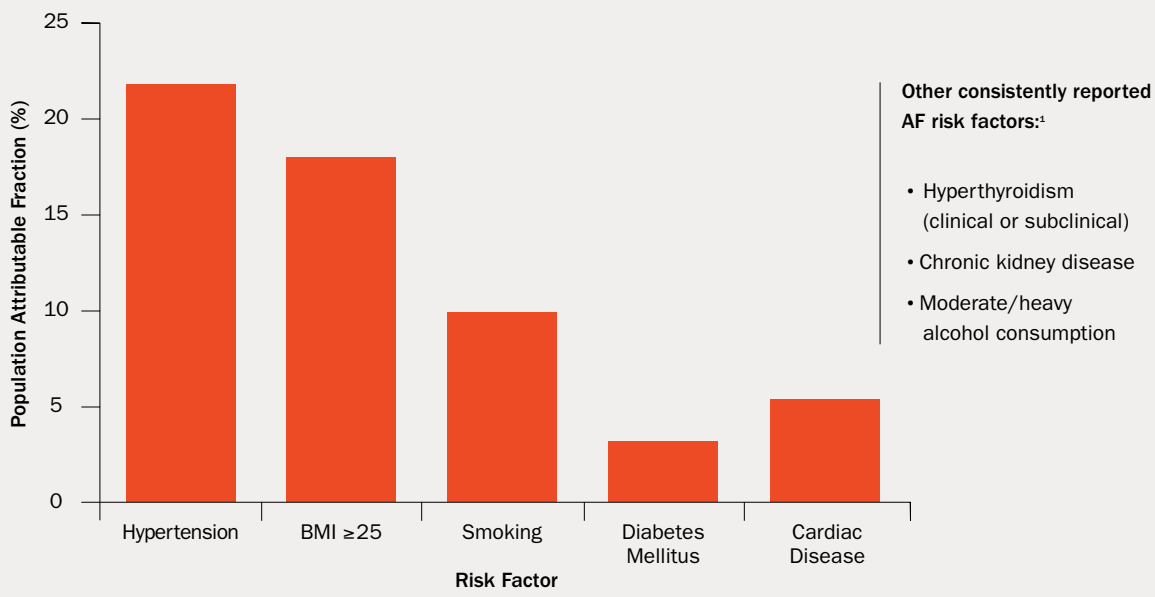
The cardiovascular consequences of AF relate to atrial/atrial appendage thrombus formation and reduced cardiac output and include stroke (three- to five-fold increased risk); sudden cardiac death, dementia, and chronic kidney disease (each associated with a two-fold increased risk); and physical disability and poor quality of life.[4] AF is also associated with increased mortality in individuals with other cardiovascular conditions, diabetes mellitus, end-stage renal disease, or sepsis and in persons undergoing cardiac or noncardiac surgery.[4]

"Early referral to a comprehensive AF center, ideally after the first episode, is key to optimizing patient outcomes," emphasizes Dr. Dandamudi.

Initial Evaluation and Treatment Options

Stable patients presenting for their first evaluation at the IU Health Methodist Hospital Atrial Fibrillation Center receive a complete history and physical examination to exclude reversible causes of AF, such as hyperthyroidism, and elucidate the presence and type of symptoms. Electrocardiographic (ECG) documentation of AF is necessary to establish the diagnosis; two-dimensional Doppler echocardiography is performed to assess heart function and rule-

Figure 1. Major risk factors for AF in the Atherosclerosis Risk in Communities Study[2]



"The three principal goals of therapy in patients with AF are reducing stroke risk, decreasing the potential for tachycardia-mediated cardiomyopathy, and alleviating symptoms."

TABLE 1. CHA_2DS_2-VASc SCORING SYSTEM FOR AF[13]

Criteria		Possible Points
Age in years <65 65–74 ≥75	 Yes Yes Yes	 0 +1 +2
Congestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	Yes	+1
Hypertension Resting BP >140/90 mmHg on ≥2 occasions or current antihypertensive pharmacologic treatment	Yes	+1
Diabetes mellitus Fasting glucose >125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	Yes	+1
Stroke, TIA, or TE Includes a history of cerebral ischemia	Yes	+2
Vascular disease Previous MI, PAD, or aortic plaque	Yes	+1
Female gender	Yes	+1

Scoring Key
0 (male) or 1 (female) = low risk of stroke
1 (male) = moderate risk of stroke
≥2 = high risk of stroke

BP = blood pressure
TIA = transient ischemic attack
TE = thromboembolism
PAD = peripheral artery disease

out structural abnormalities. Patients are also evaluated for obstructive sleep apnea, which occurs concurrent with AF in an estimated 32 to 49 percent of patients.[5]

"The three principal goals of therapy in patients with AF are reducing stroke risk, decreasing the potential for tachycardia-mediated cardiomyopathy, and alleviating symptoms," Dr. Dandamudi states. "Treatment strategies usually include antithrombotic therapy and interventions focused on rate and/or rhythm control. Lifestyle modifications, in particular weight loss and regular exercise, are strongly recommended, as both have been shown to reduce AF burden."[6]

Antithrombotic Therapy

The development and subsequent embolization of atrial thrombi can occur with any form of AF. Ischemic embolic stroke is the most frequent clinical manifestation of AF-associated embolization, but thrombi may also travel to other locations in the systemic circulation.

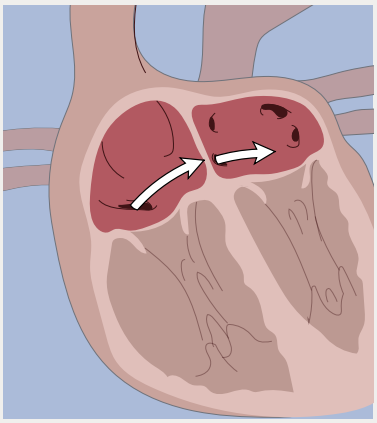
"Decisions about antithrombotic therapy are individualized, based on an assessment of stroke versus bleeding risk and consideration of patient preferences," Dr. Dandamudi says. "We use the CHA_2DS_2-VASc score *(Table 1)* to calculate a patient's risk for stroke and generally recommend oral anticoagulants when the score is 2 or higher, provided the risk versus benefit ratio supports treatment."

Controlling the Ventricular Rate

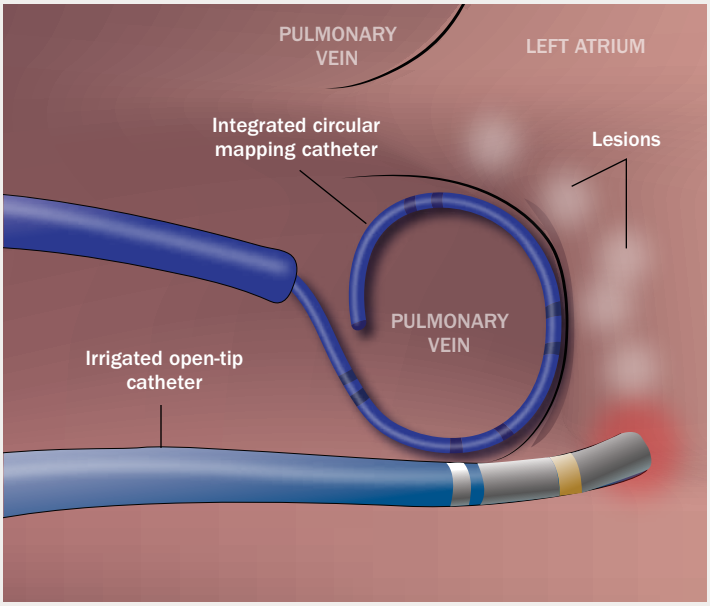
Some patients with new onset AF present with symptoms resulting from a rapid ventricular response. These individuals often experience dramatic improvement in their sense of well-being when the ventricular rate is reduced using drugs that slow conduction across the arterioventricular node, specifically beta blockers or nondihydropyridine calcium channel blockers. A resting heart rate <80 beats per minute is considered reasonable for symptomatic AF management.[3]

Figure 2. Percutaneous ablation of the pulmonary vein[12]*

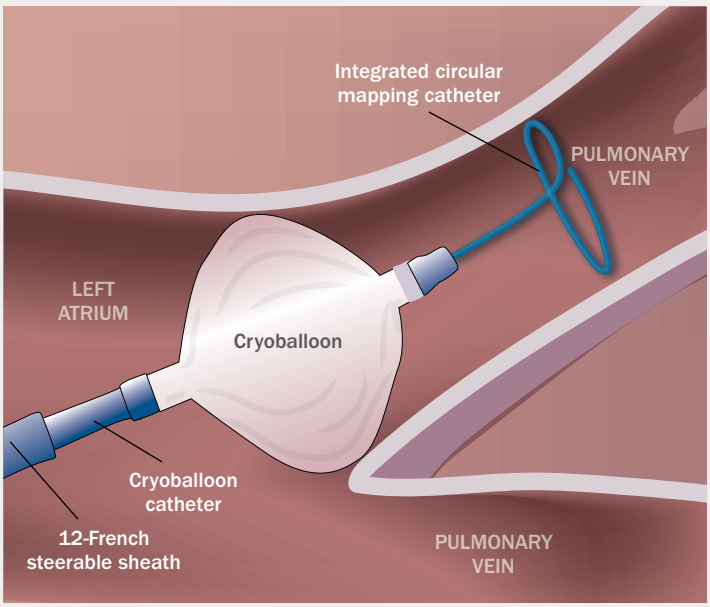
Left atrium access route



A. *Radiofrequency ablation*



B. *Cryoballoon ablation*



**The left atrium access route is used for both procedures.*

A. *The radiofrequency catheter ablation system uses heat-energy transfer to tissue and delivers a series of point-by-point connected lesions.*

B. *The cryoballoon system is a single-step approach in which a balloon delivers subzero temperatures to the pulmonary vein antra.*

Restoring and Maintaining Sinus Rhythm

In most patients, the restoration and maintenance of sinus rhythm mitigate AF symptoms by decreasing the frequency and duration of episodes.

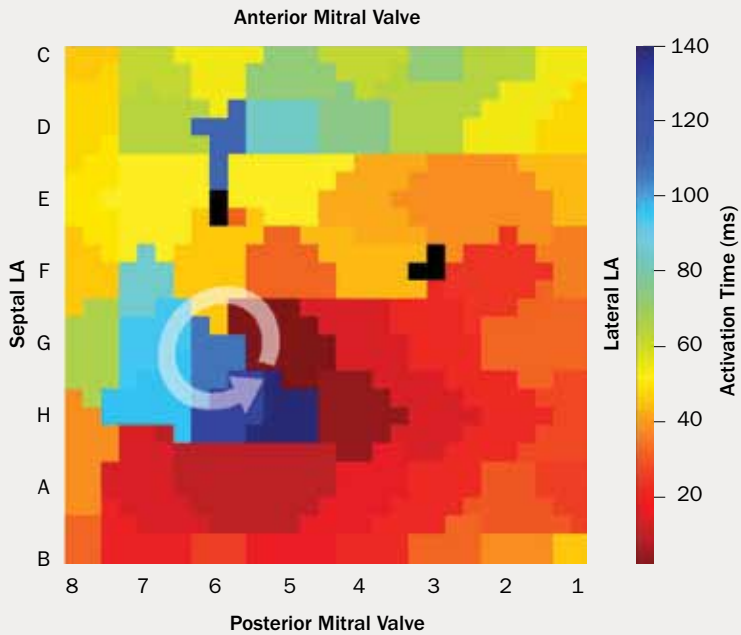
Pharmacotherapy. AADs, primarily dofetilide, dronedarone, flecainide, propafenone, and sotalol, are commonly used first-line for the management of AF symptoms. While amiodarone is more likely to maintain sinus rhythm than other AADs, it also has the highest risk for long-term side effects (e.g., lung scarring; thyroid disease; liver, eye, and skin problems). Consequently, amiodarone is typically selected for chronic use only when treatment with other antiarrhythmics has failed or is contraindicated.

Class III agents, such as dofetilide and sotalol, are linked to a 10 to 15 percent incidence of adverse cardiac events during the initiation of AAD therapy. Treatment with these drugs requires that patients be hospitalized for three days for continuous ECG monitoring. Because drug effectiveness declines over time, a second AAD may be substituted for the first if AF recurs with unacceptable frequency.

Catheter ablation. "Ablation is another strategy for rhythm control in symptomatic AF," reports Dr. Dandamudi. "Although ablation has traditionally been employed second-line in those refractory to or intolerant of antiarrhythmic medications, we are increasingly using it as initial therapy for selected patients with PAF based on clinical trial data showing long-term efficacy in this setting."[7-10]

Figure 3. FIRM mapping before AF ablation

FIRM mapping showing rotational activity.



Percutaneous Catheter Ablation

Percutaneous catheter ablation in the vicinity of the pulmonary veins was first described as a treatment for AF in 1998.[11] Today, ablation is performed using radiofrequency or a cryoballoon and causes tissue necrosis via heating or freezing, respectively *(Figure 2)*. Results of a randomized clinical trial that enrolled 762 patients with drug-refractory PAF followed for a mean duration of 1.5 years found the two techniques were comparably safe and effective.[12]

Focal Impulse and Rotor Modulation (FIRM) Ablation

"Pulmonary vein isolation (PVI) is the cornerstone of AF ablation, with the goal of eliminating the electrical mechanisms triggering arrhythmic episodes," Dr. Dandamudi explains. "However, some triggers are located outside the pulmonary veins—for example, certain substrates in the atria can perpetuate AF. FIRM ablation has the potential to precisely map, target, and eliminate these electrical sources (called rotors because of their circular shape and spinning motion) using proprietary* three-dimensional electrophysiologic mapping software and catheters *(Figure 3)* combined with radiofrequency or cryoballoon ablation."

IU Health is one of only two centers in Indiana offering FIRM ablation for the management of AF. Additionally, the IU School of Medicine Krannert Institute of Cardiology is participating in two multicenter clinical trials to further evaluate this therapeutic modality. Dr. Dandamudi is the principal investigator for the REAFFIRM trial (NCT02274857), which is reassessing the efficacy of FIRM for *de novo* AF ablation. His IU Health colleague, John Miller, MD, heads the REDO-FIRM trial (NCT02799043), which is studying FIRM in individuals undergoing repeat ablation for AF recurrence. Both trials are currently recruiting adult patients. For more information, please contact Susan Straka, RN at 317-274-0986.

**Topera® Physiologic Rotor Mapping Solution, Abbott.*

Because of the frequency of PAF episodes, the patient is considered a good candidate for percutaneous catheter ablation, and PVI is determined to be the best approach. During the two-hour procedure, performed under general anesthesia, all four pulmonary veins are isolated, and AF ablation is accomplished using a cryoballoon. She is monitored in the hospital overnight and discharged home the following morning. Flecainide is discontinued.

At one-month follow-up, the patient reports she has not experienced any AF symptoms and has resumed daily exercise that includes bicycle riding. Her heart rhythm is monitored continuously through a small wireless device* implanted in the upper chest area, allowing her physician to identify arrhythmia recurrence and to adjust her medication regimen accordingly. If no AF episodes occur over the next two months, anticoagulation will be discontinued.

Proactive AF Monitoring

Proactive patient monitoring is revolutionizing AF management, according to Dr. Dandamudi.

"Wireless devices that attach directly to smartphones, and soon-to-become available devices incorporated into smartwatches, allow patients to capture a medical-grade ECG in just a few seconds," he concludes. "These data can then be transmitted electronically to the healthcare team for assessment and guidance, resulting in timely changes to the treatment plan, when necessary.

At one-month follow-up, the patient reports she has not experienced any AF symptoms and has resumed daily exercise that includes bicycle riding.

For more *Advanced Praxis*, visit iuhealth.org/ap

For free CME credit, visit iuhealth.org/ap and click on CME Credit Form

*Medtronic Reveal LINQ™, which is one-third the size of a AAA battery and provides cardiac monitoring for up to three years.

Gopi Dandamudi, MD

Electrophysiologist, IU Health

Director of the Atrial Fibrillation Center, IU Health

Assistant Professor of Medicine, IU School of Medicine

gdandamu@iuhealth.org

Dr. Dandamudi received his medical degree from the Ross University School of Medicine in Miramar, FL and did his residency training in internal medicine at IU School of Medicine, where he also completed fellowships in cardiology and cardiovascular medicine. His clinical interests are focused on cardiology and cardiac electrophysiology, and he serves as the system-wide medical director of IU Health Cardiac Electrophysiology and program director of the Atrial Fibrillation Center.

A fellow of the Heart Rhythm Society and member of the American College of Cardiology, Dr. Dandamudi is the principal or a co-investigator for several ongoing AF clinical trials. He is also the author of numerous peer-reviewed publications and textbook chapters, an editorial board member of the journal *Heart Rhythm*, and lectures extensively at medical symposia in the United States and abroad.

Dr. Dandamudi is currently pursuing a masters in business administration with a concentration in healthcare at Ball State University. He expects to receive his degree in 2018.

References

1. Centers for Disease Control and Prevention. Atrial fibrillation fact sheet. Available at: https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm.
2. Huxley RR, Lopez FL, Folsom AR, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study. *Circulation*. 2011;123(14):1501-1508.
3. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation*. 2014;130(23):2071-2104.
4. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation*. 2016;133(4):e38-360.
5. Todd K, McIntyre WF, Baranchuk A. Obstructive sleep apnea and atrial fibrillation. *Nat Sci Sleep*. 2010;2:39-45.
6. Pathak RK, Elliott A, Middeldorp ME, et al. Impact of CARDIOrespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation: The CARDIO-FIT Study. *J Am Coll Cardiol*. 2015;66(9):985-996.
7. Nielsen JC, Johannessen A, Raatikainen P, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. *N Engl J Med*. 2012;367(17):1587-1595.
8. Nielsen JC, Johannessen A, Raatikainen P, et al. Long-term efficacy of catheter ablation as first-line therapy for paroxysmal atrial fibrillation: 5-year outcome in a randomised clinical trial. *Heart*. 2016.
9. Raatikainen MJ, Hakalahti A, Uusimaa P, et al. Radiofrequency catheter ablation maintains its efficacy better than antiarrhythmic medication in patients with paroxysmal atrial fibrillation: On-treatment analysis of the randomized controlled MANTRA-PAF trial. *Int J Cardiol.* 2015;198:108-114.
10. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJ. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. *Europace.* 2015;17(3):370-378.
11. Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med.* 1998;339(10):659-666.
12. Kuck KH, Brugada J, Furnkranz A, et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *N Engl J Med.* 2016;374(23):2235-2245.
13. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest.* 2010;137(2):263-272.

IU Health Physicians

340 West Tenth Street, FS 5100
Indianapolis, IN 46202

IU Health Physicians is the most complete, multi-specialty practice group in Indiana. A unique partnership between Indiana University School of Medicine faculty physicians and private practice physicians, IU Health Physicians gives its highly skilled doctors access to innovative treatments using the latest research and technology.

We hope that you find each topic's case management to be informative and valuable. If you have any questions, we welcome you to contact either *Advanced Praxis* or the featured physician at the numbers/email addresses below.

Referral information: 1-800-622-4989 or iuhealth.org/find-a-doctor

Dr. Gopi Dandamudi, featured physician: gdandamu@iuhealth.org

Kara Anderson, publisher of *Advanced Praxis*: advancedpraxis@iuhealth.org