

# Clinical Management of the Patient with Atrial Fibrillation

## ACUTE TREATMENT

The acute management of atrial fibrillation (AF) can be challenging and complex. AF is often associated with other conditions such as myocardial ischemia or pneumonia which result in more difficult rate control and concomitant hemodynamic difficulty. The patient's volume status can be difficult to assess. Patients may present with dehydration due to elevated levels of atrial natriuretic peptide or volume overload in heart failure.

Additionally, in the acute setting, AF can be very rapid and often appear regular. Careful examination of the electrocardiography (ECG) is important to differentiate AF from other supraventricular arrhythmias. The initial assessment of the patient is important in determining the course of therapy.

Identification of the possible cause/trigger of acute AF is important to the management. One of the more common clinical settings for acute onset AF is the post coronary bypass recovery period. After coronary revascularization, the incidence of AF is about 19%.<sup>1</sup> This risk peaks between post-operative days 2 to 5. Other acute causes of AF include the infusion of catecholamines or other stimulants such as cocaine. Excessive ethanol ingestion also can result in acute onset AF. Changes in atrial pressure can acutely induce AF. Patients with pneumonia or pulmonary embolism can present with AF. Because of the elevated sympathetic tone seen with these conditions, AF may be difficult to control. Additionally, beta blockers may be difficult to give to patients with lung disease who are actively wheezing. Chronic elevations in atrial pressure can also induce AF. Patients with obstructive sleep apnea, chronic obstructive pulmonary disease, hypertension, heart failure, acute myocardial infarction or valvular heart disease can present with AF.

Patients with mitral stenosis depend on atrial systole and longer ventricular filling times to maintain stroke volume. Thus, treatment of AF in patients with mitral stenosis can be an emergency. Thyrotoxicosis can cause rapid AF that may be difficult to control. Beta blockers are the treatment of choice; digoxin may be ineffective in this situation.

When a patient presents with AF, rate control should be the first line of therapy. Controlling the rate will improve stroke volume by increasing the diastolic filling time. Additionally, rate control will aid in controlling ischemia and heart failure symptoms. The mainstays for initial heart rate control include diltiazem and beta blockers. Esmolol is a short acting beta blocker that has been used in acute AF management. The initial bolus is 0.5 mg/kg intravenously followed by 0.05 mg/kg which can be titrated up to 0.2 mg/kg with additional boluses.<sup>2</sup> Diltiazem has also been used for acute intravenous control of AF. The initial bolus is 0.25 mg/kg intravenously with a maintenance infusion of 5 mg/hr. which can be titrated up to 20 mg/hr.<sup>2</sup> The choice of the drug should be based on the concomitant clinical conditions. For example, beta blockers should be avoided in patients with acute asthma. These same drugs, however, would be appropriate in the setting of myocardial ischemia. In a study

comparing diltiazem and esmolol in patients with AF after coronary artery bypass surgery, diltiazem was more effective at achieving rate control within 12 hours; conversely, esmolol was associated with successful conversion to sinus rhythm compared to diltiazem.<sup>3</sup> Digoxin and amiodarone can be used in patients with heart failure. In settings of high sympathetic tone, digoxin may not be very effective in controlling heart rate. It should be noted that when administered intravenously, amiodarone can result in hypotension. (*Refer to Table 1*).

In some circumstances, conversion to sinus rhythm may be the best way to achieve rate control. Patients with ischemia or significant hemodynamic consequences of AF may be candidates for cardioversion. In general, direct current cardioversion is safe in patients who have been NPO for eight hours if the duration of their AF is less than 48 hours. Beyond this, in patients with severe ischemia or hemodynamic compromise, the risks of both anesthesia and thromboembolism must be considered. Chemical cardioversion can be considered in patients where anesthesia is either unavailable or unsafe. Ibutilide, a Class III antiarrhythmic, is the most commonly used agent for pharmacological conversion of AF. Ibutilide is a potassium channel blocker, prolongs the action potential and increases atrial refractoriness resulting in restoration of sinus rhythm. Potassium channel blockers also are associated with torsades de pointes. In one study, ibutilide was significantly more effective in converting patients with AF or flutter to normal sinus rhythm when compared to procainamide.<sup>4</sup> The dose of ibutilide is 1 mg intravenously over ten minutes, and may be repeated. The QT interval should be monitored during and after this infusion.

In patients whose AF duration is greater than 48 hours, anticoagulation with heparin and subsequently with an oral anticoagulant should be considered, regardless of the method of conversion. The patient should receive anticoagulation for 3 consecutive weeks prior to attempted cardioversion with a target INR of 2.0-3.0 (if warfarin is used). Anticoagulation should be maintained for 4 weeks post successful cardioversion.<sup>5</sup>

**TABLE 1. Drug Therapy for HR Control in AF: Acute Management**

Drug	Loading Dose	Onset	Maintenance Dose	Major Adverse Effects
<b>PATIENTS WITHOUT ACCESSORY PATHWAY</b>				
Esmolol	500 µg/kg IV over 1 min	5 min	60-200 µg/kg/min IV	↓BP, HB, ↓HR, asthma, HF
Metoprolol	2.5-5 mg IV bolus over 2 min; up to 3 doses	5 min	NA	↓BP, HB, ↓HR, asthma, HF
Diltiazem	0.25 mg/kg IV over 2 min	2-7 min	5-15 mg/h IV	↓BP, HB, HF
Verapamil	0.075-0.15 mg/kg IV over 2 min	3-5 min	NA	↓BP, HB, HF
<b>PATIENTS WITH ACCESSORY PATHWAY</b>				
Amiodarone	150 mg over 10 min	Days	0.5-1 mg/min IV	↓BP, HB, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction, sinus bradycardia
<b>PATIENTS WITH HEART FAILURE AND WITHOUT ACCESSORY PATHWAY</b>				
Digoxin	0.25 mg IV q2 h, to 1.5 mg	≥60 min	0.125-0.375 mg/d IV or po	Digitalis toxicity, HB, ↓HR
Amiodarone	Dosing, onset, and major adverse effects as above			
BP=blood pressure; HB=heart block; HR heart rate; HF=heart failure Source: American Heart Association, Inc.				

Because AF shortens the atrial refractory period, recurrence of the arrhythmia is common after conversion to sinus rhythm. Thus, treatment with antiarrhythmic drugs may be needed to maintain sinus rhythm after acute cardioversion.

## CHRONIC MANAGEMENT

### Factors involved in clinical recommendations

The basic principles of therapy for patients with AF include:

1. risk stratification and prevention of thromboembolic complications of stroke (discussed in detail in an accompanying article by Parra and Long)
2. ventricular rate control, if expedient restoration and maintenance of sinus rhythm is not contemplated
3. pharmacologic or electrical restoration and maintenance of sinus rhythm
4. choice of an appropriate long-term rhythm control strategy and identification of AF amenable to ablation
5. identification and correction of risk factors and eradication of precipitating agents
6. treatment of underlying pathology.<sup>6</sup>

Medical therapy remains the mainstay for treatment for the majority of patients with AF. The optimal management strategy for the individual AF patient is contingent on the underlying condition. The presence or absence of structural heart disease (SHD) will influence both the approach to patient management

(rate vs. rhythm control) and the treatment options available. Rate control refers to control of the ventricular rate during AF without an attempt to restore sinus rhythm. Rhythm control refers to restoring and maintaining sinus rhythm. Upstream therapies refer to drug therapy that helps to maintain sinus rhythm but are not considered antiarrhythmic.<sup>7</sup>

Several basic tenets should be considered when selecting a management strategy. They include the following:<sup>8</sup>

- no patient wants to be in AF
- a stable rhythm is largely better than an unstable rhythm
- new onset AF is a high-risk period
- development of AF generally indicates a worse prognosis than most serious diseases
- stroke risk must be addressed
- safety should determine the initial antiarrhythmic drugs (AAD) selected for rhythm control
- therapy for underlying conditions should be optimal and guideline based.

To facilitate clinical decisions regarding management of patients with AF, the American College of Cardiology (ACC), the American Heart Association (AHA) and the European Society of Cardiology (ESC) developed joint guidelines for optimal pharmacologic and interventional approach to AF in 2006.<sup>2</sup> The ACC/AHA and the Heart Rhythm Society (HRS) published a 2011 focused guideline update at the end of 2010,<sup>9</sup>

and a second update in 2014<sup>10</sup>. As outlined in the guidelines, the rate control strategy emphasizes the utilization of medications to control the ventricular rate with no attempt to achieve rhythm control. The rhythm control strategy focuses on restoration and maintenance of sinus rhythm through AAD therapy. These approaches are based on data from randomized clinical trials.

The major clinical trials to evaluate rate vs. rhythm control include the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)<sup>11</sup>, the Rate Control Versus Electrical Cardioversion (RACE) Trial<sup>12</sup>, RACE II<sup>13</sup>, and the Atrial Fibrillation Congestive Heart Failure (AF-CHF) trials.<sup>14</sup> Other studies which focused on this issue include the Pharmacological Intervention in Atrial Fibrillation (PIAF)<sup>15</sup>, Strategies of Treatment of Atrial Fibrillation (STAF)<sup>16</sup>, and How to Treat Chronic Atrial Fibrillation (HOT CAFÉ)<sup>17</sup>.

The AFFIRM study<sup>11</sup>, which evaluated mortality benefit of different strategies in AF, included 4060 AF patients ≥ 65 years of age with at least one risk factor for stroke. The mean follow-up was 3.5 years, with a maximum of 6 years. There was no difference in the primary endpoint of all-cause mortality as well as quality of life and functional status between rate and rhythm control. However, this trial included an elderly population and clearly did not include young, active or

highly symptomatic patients. Interestingly, a post hoc analysis of the AFFIRM trial, after correction for any mismatch of baseline characteristics, demonstrated that being in sinus rhythm was an advantage but the use of AAD was associated with an increased risk of death.<sup>18</sup>

The AF-CHF trial<sup>14</sup> included 1376 NYHA class II–IV heart failure patients with a LVEF ≤ 35% and randomized patients to either a rate vs. rhythm-control strategy. Amiodarone was the drug of choice for AF suppression and sinus rhythm maintenance, and sotalol and dofetilide were used in selected cases. The study revealed no benefit of rhythm control in addition to optimal medical therapy with regard to the primary endpoint (cardiovascular mortality) as well as prespecified secondary endpoints, including total death, worsening heart failure, stroke, and hospitalization.

The RACE trial<sup>12</sup> included 522 patients with persistent AF, who had a prior cardioversion and were currently in AF. Patients were randomized to a strategy of repeat cardiover-

sion and AAD to maintain sinus rhythm or to pharmacologic rate control. The primary end point was a composite of cardiovascular death, heart failure, thromboembolism, bleeding, pacemaker insertion, or severe side effects of antiarrhythmic drugs. The end point did not differ between the 2 groups at a mean follow-up of 2.3 years. Analysis of quality of life, a secondary end point, showed no difference between these 2 strategies. The RACE II study which included 614 patients with permanent AF, also found no significant difference in clinical outcomes including cardiovascular mortality, hospitalization for CHF, stroke, major bleeding, ventricular tachyarrhythmias, between lenient (resting heart rate < 110 beats/min) and strict (resting heart rate < 80 beats/min and heart rate during moderate exercise < 110 beats/min) rate control (12.9% vs. 14.9%). AF was treated with a variety of atrioventricular (AV) nodal blocking agents to control heart rate.<sup>12</sup>

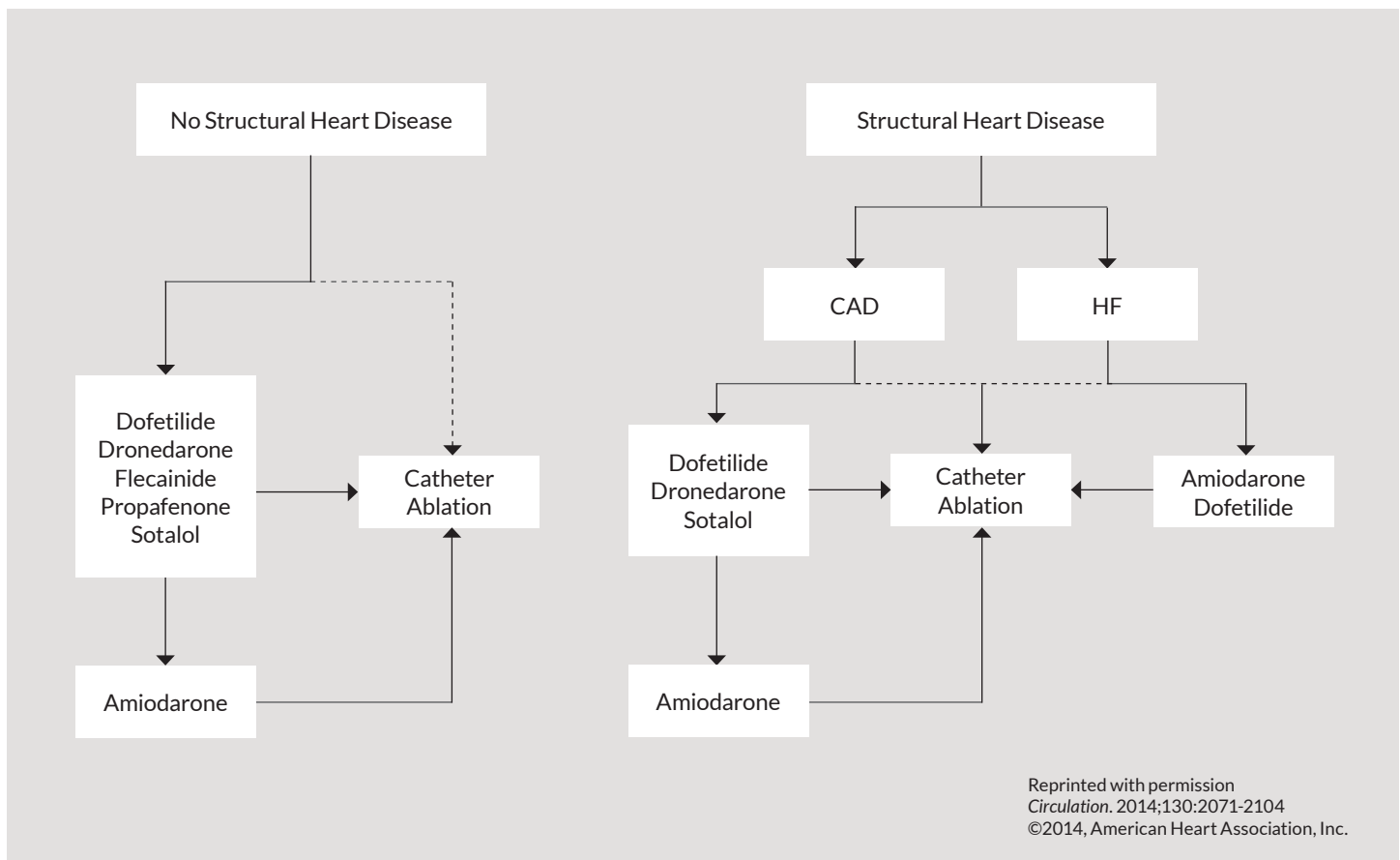
The PIAF, STAF AND HOT CAFÉ studies revealed a trend for improved survival and lower cardiovascular adverse events with rate

control rather than rhythm control. Overall, these studies demonstrate that choosing a rate control or rhythm control strategy for a patient should be based on symptoms and a thorough discussion of the risks and benefits of each should be undertaken.

#### PHARMACOLOGIC: Maintenance of Sinus Rhythm

Rhythm control is instinctively a more attractive option because it offers physiologic rate control, normal atrial contraction and activation, the appropriate sequence of AV activation, normal hemodynamics and AV valve function and theoretically eliminates factors that encourage thrombosis within the atria and embolization of blood clots.<sup>6</sup> Restoration and maintenance of sinus rhythm should be strongly considered for most symptomatic patients with paroxysmal and persistent AF.<sup>9,10</sup> Other factors favoring rhythm control include younger patients, tachycardia induced cardiomyopathy, first episode of AF, difficulty in achieving adequate rate control, AF that was precipitated by an acute illness and patient's

**FIGURE. Strategies for rhythm control in patients with paroxysmal and persistent AF**



**TABLE 2. Pharmacologic Therapy to Maintain Sinus Rhythm: Typical Dosages and Adverse Effects**

Drug	Daily Dose	Major Adverse Effects
Amiodarone	100-400 mg	Photosensitivity, pulmonary toxicity, polyneuropathy, GI upset, bradycardia, torsades de pointes (rare), hepatic toxicity, thyroid dysfunction, eye complications
Disopyramide	400-700 mg	Torsades de pointes, HF, glaucoma, urinary retention, dry mouth
Dronedareone	800 mg	New or worsening heart failure, QT prolongation, bradycardia
Dofetilide	500-1000 µg	Torsades de pointes
Flecainide	200-300 mg	VT, HF, conversion to atrial flutter with rapid conduction through the AV node
Propafenone	450-900 mg	VT, HF, conversion to atrial flutter with rapid conduction through the AV node
Sotalol	160-320 mg	Torsades de pointes, HF, bradycardia, exacerbation of chronic obstructive or bronchospastic lung disease

GI=gastrointestinal; VT=ventricular tachycardia.  
Source: American Heart Association, Inc.

preference.<sup>10</sup> Prophylactic AAD treatment is often required. The 2014 AF guidelines<sup>10</sup> recommend that rhythm control therapy must be individualized and that before initiating AAD therapy, treatment of precipitating or reversible causes of AF should be commenced.

However, AAD have limited efficacy and considerable unattractive adverse effects.<sup>19</sup> The goal of maintenance therapy is suppression of symptoms and at times, prevention of tachycardia-induced cardiomyopathy due to AF with a rapid ventricular response.<sup>9,10</sup> Atrial fibrillation recurrence is not equivalent to treatment failure, since most patients experience recurrence. A reduction in AF burden constitutes a partial success.<sup>9,10</sup> Consideration of underlying structural heart disease is essential for the selection of an AAD. *Figure 1* from the ACC/AHA/HRS 2014 updated guidelines is a summary of therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. 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. Drugs are not in order of suggested use but are listed alphabetically.<sup>9</sup>

Beta blockers are usually effective in patients with exercise induced AF or lone AF. Flecainide, propafenone and sotalol are also effective in these patients without SHD. Amiodarone and dofetilide are used as alter-

native therapies. Patients with heart failure have fewer AAD options compared to those without SHD.

The primary pharmacologic agents for rhythm control in patients with HF are the class III AAD; however HF patients are prone to the proarrhythmic effects of AAD. Amiodarone has the greatest efficacy for maintenance of sinus rhythm but carries the potential for noncardiac toxicities. Amiodarone can prolong the QT interval and cause bradycardia, but rarely causes ventricular proarrhythmia. Dofetilide is reasonably safe and effective for HF patients.<sup>20</sup> Dronedarone is moderately effective in maintaining sinus rhythm and has ventricular-rate slowing properties when AF recurs, however, dronedarone is not recommended in patients with NYHA class IV HF<sup>21</sup> or in patients with permanent AF.<sup>22</sup>

In stable patients with coronary artery disease, beta blockers should be considered. Sotalol has beta blocking activity and can also be used for initial AAD therapy. Patients with LVH are at an increased risk for ventricular proarrhythmia; first line therapy should be an AAD that does not prolong the QT interval. Since the rate of torsades de pointes with class III agents is 0.9% to 3.3%<sup>23</sup>, in hospital initiation of AAD therapy is recommended for quinidine, procainamide, sotalol, and dofetilide. Generally, AAD should be started at a lower

dose with upward titration, reassessing the ECG with dose changes or if concomitant drug therapies are introduced. (*Refer to Table 2 for drug dosing and adverse effects.*)

### PHARMACOLOGIC: Rate Control

A primary strategy of rate control should be considered in the following patients<sup>6,9,10</sup>:

- Those with a permanent form of the arrhythmia associated with mild symptoms that can be improved by slowing heart rate
- Those patients ≥ 65 years age with recurrent AF when the AF is accepted by the patient and the provider
- Those with persistent AF with failed repeat cardioversions and serial prophylactic AAD and in whom the risk/benefit ratio from using specific antiarrhythmic agents leans toward increased risk or those who are ineligible for ablation therapy.

The ventricular rate during AF may accelerate excessively during exercise even if it is well controlled at rest. Ventricular rate reduction allows sufficient time for ventricular filling, avoids rate-related ischemia, and may improve hemodynamics. Criteria for rate control vary with patient age but usually involve achieving ventricular rates during AF between 60-80 bpm at rest and between 90-115 bpm during moderate exercise.<sup>9,10</sup> Generally beta blockers are the most common drugs used for rate control, followed by nondihydropyridine calcium channel blockers, digoxin and amiodarone.<sup>10</sup> Digoxin is effective in controlling ventricular rates at rest by prolongation of AV node conduction and refractoriness through vagal stimulation. However during exercise, most of the vagal tone is lost and the effect of digoxin is negated. Therefore, digoxin as monotherapy may be effective in elderly, sedentary patients, but a combination with beta blockers or calcium antagonists is often necessary to achieve rate control in the majority of patients. Nondihydropyridine calcium antagonists and beta blockers are also effective as primary pharmacologic therapy for rate control; however, multiple changes of drug type and dosage and/or a combination of two drugs may be needed to achieve the desired result. Amiodarone can be useful to control ventricular response but adverse effects should be considered. (*Refer to Table 3 for drug dosing and adverse effects.*) Comorbidities of patients must be appreciated in order to prevent exacerbation of chronic obstructive pulmonary disease, heart failure or conduction acceleration in patients with pre-excitation.<sup>10</sup>

**TABLE 3. Drug Therapy for HR Control in AF: Long-Term Management**

Drug	Loading Dose	Onset	Maintenance Dose	Major Adverse Effects
<b>HEART RATE CONTROL</b>				
Metoprolol	Same as maintenance dose	4-6 h	25-100 mg bid, po	↓BP, HB, ↓HR, asthma, HF
Propranolol	Same as maintenance dose	60-90 min	80-240 mg/d in divided doses, po	↓BP, HB, ↓HR, asthma, HF
Diltiazem	Same as maintenance dose	2-4 h	120-360 mg/d in divided doses, po	↓BP, HB, HF
Verapamil	Same as maintenance dose	1-2 h	120-360 mg/d in divided doses, po	↓BP, HB, HF, digoxin interaction
<b>HEART RATE CONTROL PATIENTS WITH HEART FAILURE AND WITHOUT ACCESSORY PATHWAY</b>				
Digoxin	0.5 mg/d po	2 days	0.125 to 0.375 mg/d po	Digitalis toxicity, HB, HR, ↓BP, ↓HB, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction, sinus bradycardia
Amiodarone	800 mg/d for 1 wk, po 600 mg/d for 1 wk, po 400 mg/d for 4-6 wk, po	1-3 wk	200 mg/d po	

Source: American Heart Association, Inc.

Upstream therapies refer to the use of non-antiarrhythmic medications that alter the atrial substrate or target mechanisms specific to AF to prevent recurrence. They include ACE inhibitors, angiotensin receptor blockers, aldosterone antagonists, statins, and fish oil.<sup>25</sup> These therapies target structural changes in the atria, such as fibrosis, hypertrophy, inflammation, and oxidative stress; however, direct and indirect effects on atrial ion channels, gap junctions, and calcium handling also occur.<sup>6</sup>

### Ablation and Device Therapy

Since the early 1990s, it has been recognized that triggering or initiation of AF occurs predominantly from the pulmonary veins, and that the electrical isolation of those veins could prevent AF.<sup>26</sup> The technique involves puncturing the interatrial septum with one to two catheters and delivering radiofrequency or other energy in an encircling manner around the pulmonary veins, thereby preventing triggering beats from entering the atrium. The procedure is generally safe and is increasingly being employed in the treatment of AF. Nurses and advanced practice nurses should understand the indications for the procedure and the associated complications. While there are many theoretical benefits from treating AF with ablation, the elimination of AF symptoms is the only indication that has been proven in randomized clinical trials. Thus, the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society 2012 Consensus

Statement lists “Symptomatic AF refractory to or intolerant to at least one Class I or Class III antiarrhythmic medication” as a Class I indication for ablation.<sup>27</sup> The success rate of this technique ranges from 66% to 89%.<sup>27</sup> The success rate is lower in patients with longer duration of AF, enlarged left atria and persistent versus paroxysmal AF. While this procedure is generally safe, there are several important complications to recognize. Because ablation of AF is performed in the left atrium, there is a risk of thrombus or char formation which could result in stroke or systemic embolization in 0-7% of patients.<sup>27</sup> After AF ablation, patients require frequent monitoring of neurological status. This risk of stroke is minimized by anticoagulation with heparin. However, because of anticoagulation, the risk of cardiac perforation and tamponade are increased (1.2% to 2.4%).<sup>27</sup> While tamponade usually occurs acutely in the ablation laboratory, it must be recognized early and treated with reversal of anticoagulation therapy and percutaneous or surgical evacuation of blood from the pericardium. Complications which occur later in the post-ablation period include atrio-esophageal fistulae, which occur as a result of heating of the esophagus. This complication is associated with a high mortality if not recognized immediately. Pulmonary vein stenosis can occur as a result of ablation within or too close to the pulmonary vein ostium. Additionally, patients with AF ablation may experience rapid atrial flutter after ablation. Although ablation of AF is an effective technique for

rhythm control, close monitoring of these patients in the post-operative period is required to minimize complications.

### CONCLUSION

As a collaborative team, the physician and the advanced practice nurse (APN) are committed to providing quality care for the AF patient through a comprehensive approach to patient education, problem solving, goal setting and shared decision making. (see related article by Hughes for further discussion on shared decision making).<sup>28</sup> In the setting of treating patients with AF, the physician and APN are most effective when they work collaboratively and interdependently.<sup>29</sup> Customization of treatment will be based on the patient’s needs, symptoms during recurrence of AF, and the AF burden. The APN can customize treatment for the AF patient, such as medication titration, as well as manage other co-morbidities, including hypertension and heart failure. The APN can improve patient functioning and self-management, reduce complications of treatment, decrease fragmentation of care, adhere to regulatory standards, and develop patient care processes that are supported by evidence-based guidelines. ■

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