

Management of Atrial Fibrillation: Focus on Catheter-Based Ablation

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Atrial fibrillation (AF) contributes to considerable morbidity, with increasing risk of stroke, complications from anticoagulation, and exacerbation of heart failure. AF ablation has become a commonly performed procedure in many hospitals as the procedural techniques evolve rapidly with improved success. Here we discuss the interventional options of catheter-based AF ablation for rhythm control, which offers the benefit of mortality reduction associated with normal sinus rhythm but without medication complications.

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With the aging population, atrial fibrillation (AF) prevalence is growing rapidly and is almost 6% in those over the age of 65 years and nearly 10% in those over age 85 years.¹ AF contributes to considerable morbidity, with increasing risk of stroke, complications from anticoagulation, and exacerbation of heart failure. A previous article (Schapira JN, Voroshilovsky O. *Rev Cardiovasc Med*. 2010;11:1-12) reviewed the medical management of AF. When rhythm control is chosen as the treatment option, antiarrhythmic drugs (AADs) may relieve symptoms and improve quality of life (QoL) when sinus rhythm is maintained, but often with many side effects and possible toxicities. Additionally, due to multiple contraindications, many patients with AF and coexistent structural heart disease are not candidates for most AADs. Here we discuss the interventional options of catheter-based AF ablation for rhythm

control, which offers the benefit of mortality reduction associated with normal sinus rhythm (NSR) but without medication complications. AF ablation has become a commonly performed procedure in many hospitals as its procedural techniques evolve rapidly with improved success. This article reviews the progress made over the past several years in AF ablation.

Currently, AF ablation is recommended as a second-line treatment

medication and who are highly symptomatic.² If physicians were to recommend an invasive procedure as first-line therapy, AF ablation should ideally not only limit symptoms, but also improve QoL, decrease the risk of stroke, minimize negative remodeling, improve heart failure symptoms, and increase survival while eliminating or minimizing the adverse effects of such therapy. However, there have been no studies to specifically determine if AF ablation

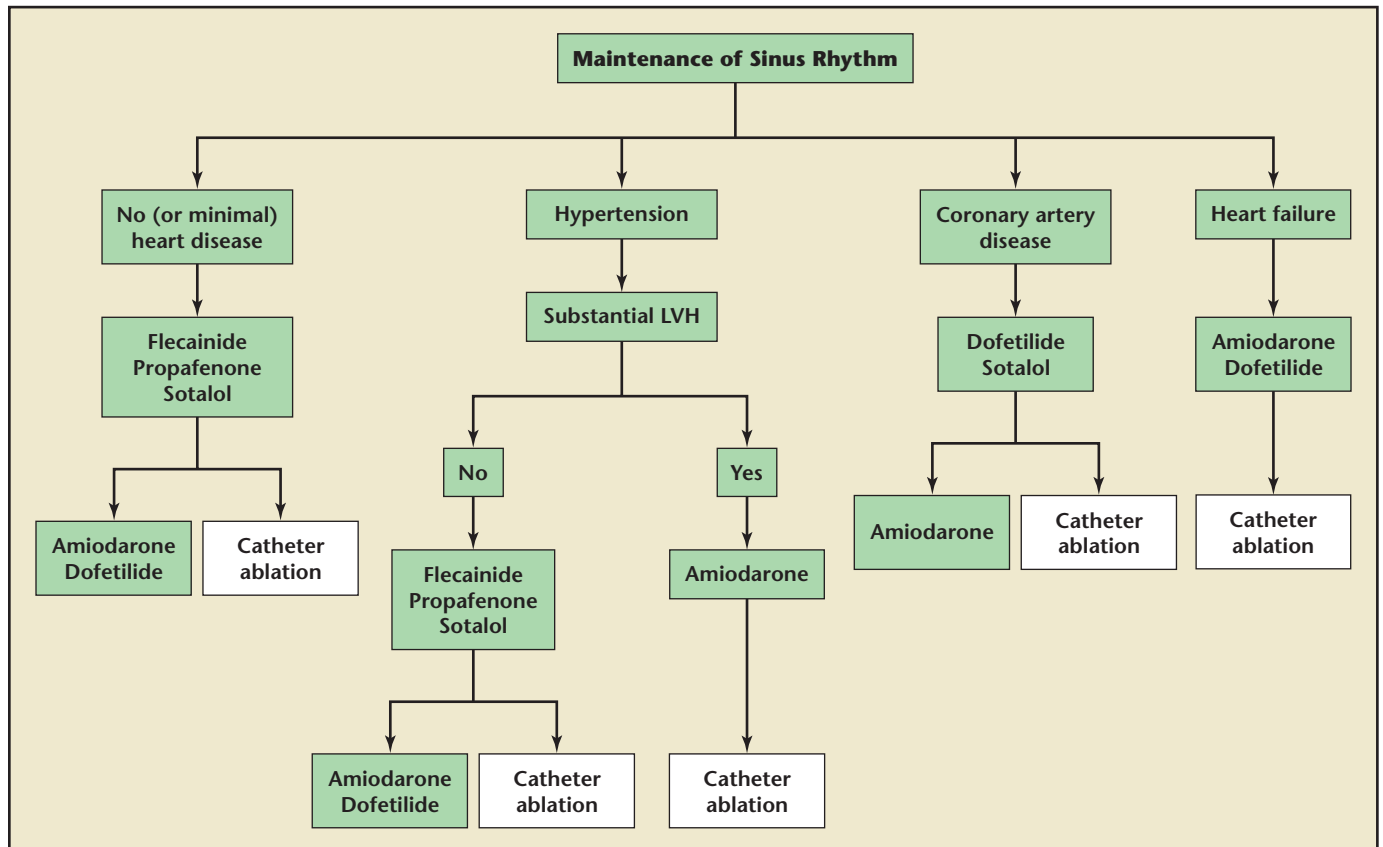
can prevent the progression to heart failure, decrease stroke rate, or impact health care costs. Prior studies (PIAF [Pharmacologic Intervention in Atrial Fibrillation], RACE [Comparison of Rate Control and Rhythm Control in Patients With Recurrent Persistent Atrial Fibrillation], STAF [Strategies of Treatment of Atrial Fibrillation], AFFIRM [Atrial Fibrillation Follow-Up Investigation of Rhythm Management]) have also not shown a mortality benefit in the maintenance of NSR when compared with rhythm control using AADs. Two small randomized clinical trials have shown an improvement in QoL with sinus rhythm restoration.^{3,4} In one, 70 patients with monthly symptomatic AF episodes were randomized to either pulmonary vein isolation (PVI) with ablation or AADs. At 1-year follow-up there were fewer

Currently, AF ablation is recommended as a second-line treatment option for patients who have failed at least 1 antiarrhythmic medication and who are highly symptomatic.

option (Figure 1) for patients who have failed at least 1 antiarrhythmic

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Figure 1. Algorithm for the maintenance of sinus rhythm based on 2006 American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) guidelines for the treatment of atrial fibrillation. LVH, left ventricular hypertrophy. Adapted with permission from Fuster V et al.²



hospitalizations in the ablation group (9%) versus the antiarrhythmic group (54%), as well as improved QoL at 6-month follow-up.³ There was also a 10% to 20% decrease in left atrial (LA) size thought to be consistent with reverse remodeling and possibly improvement in LA function.⁵ Several other small studies have also shown that in patients with heart failure and depressed ejection fraction (EF), in addition to improved QoL, there is also the added benefit of an improvement in EF and decreased left ventricular (LV) dimensions following successful AF ablation and restoration of sinus rhythm. In one such study, patients with EF < 45% and heart failure who underwent AF ablation were compared with those without heart failure; after 1 year > 70% of those with heart failure showed a marked improvement in EF to > 55%.⁴

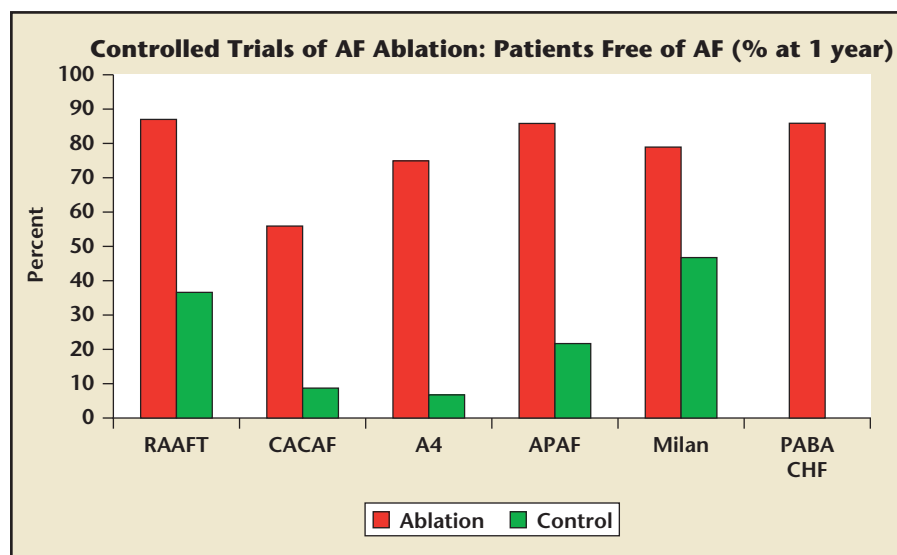
As clinicians we understand that AF has certain consequences, such as decreased cardiac stroke volume, increased LA volume, shortening of the diastolic ventricular filling period, and increased atrioventricular (AV) valvular regurgitation, and often causes an irregular, rapid ventricular rate, all of which contribute to the symptoms of AF and worsening cardiac function.⁶ Therefore, it seems that maintenance of NSR should be beneficial. A recent "on-treatment" analysis of the AFFIRM study showed that although there was no significant difference in all-cause mortality between the 2 strategies of rate and rhythm control, the presence of sinus rhythm was associated with an almost 50% reduction in risk of death (hazard ratio [HR] = 0.53).⁷ AFFIRM was a randomized trial in which patients received either rate versus rhythm control and were followed for an average of 2.6 years. The primary endpoint was total mortality. The composite of total mortality, stroke, and anoxic encephalopa-

thy, as well as functional status, QoL, and cost effectiveness, were evaluated as secondary endpoints. Similar findings were also seen in the DIAMOND (Danish Investigations of Arrhythmia and Mortality on Dofetilide) substudy assessing dofetilide treatment of AF. In this study patients with LV dysfunction and AF or atrial flutter were treated with dofetilide to maintain or restore sinus rhythm. Dofetilide had no effect on all-cause mortality, but restoration and maintenance of sinus rhythm was associated with significant mortality reduction (relative risk, 0.44).⁸ Conversely, AADs were also associated with an increased mortality in the AFFIRM substudy, as has previously been seen in the SPAF (Stroke Prevention in Atrial Fibrillation), CAST (Cardiac Arrhythmia Suppression Trial), and SWORD (Survival With Oral *d*-Sotalol) trials.⁷

This raises the question whether this benefit of NSR in most studies was offset by the potentially harmful side effects of AAD therapy. Therefore, a treatment that is effective in maintain-

ing NSR but has minimal adverse effects may show a clear benefit. The confirmation of such benefit was seen in a small study of AF ablation using circumferential PVI that did show symptomatic relief without increasing mortality (as AADs do) in patients with symptomatic AF. In this study, 1171 patients were evaluated, 589 underwent ablation, and 582 received AADs. With median follow-up of 900 days, observed survival was longer in patients treated with ablation than in patients treated medically ($P < .001$), with an HR of 0.46 for all-cause mortality and an HR of 0.45 for morbidities, mainly due to heart failure and ischemic cerebrovascular events. Hazard ratio for AF recurrence was 0.30.⁹ Additionally, several other small studies have compared circumferential PVI with AAD therapy and have shown superior prevention of recurrent AF, as well as improved morbidity and mortality (Figure 2).^{3,10-12} However, large prospective, multicenter, randomized studies are still needed to assess efficacy of catheter ablation for AF.

Figure 2. Results of diverse controlled trials on catheter ablation of atrial fibrillation (AF). A4, Atrial Fibrillation Ablation Versus Antiarrhythmic Drugs; APAF, Ablation for Paroxysmal Atrial Fibrillation; CACAF, Catheter Ablation for the Cure of Atrial Fibrillation; PABA CHF, Pulmonary Vein Atrium Isolation vs AV-Node Ablation With Bi-Ventricular Pacing for Treatment of Atrial Fibrillation in Patients With Congestive Heart Failure, RAAFT, Radiofrequency Ablation of Atrial Fibrillation Trial. Reprinted from Am J Cardiol, Vol. 109, d'Avila and Ruskin, Nonpharmacologic strategies: the evolving story for ablation and hybrid therapy, pages 20H-24H, copyright © 2008, with permission from Elsevier.



Such studies are difficult to design because of the extensive variability not only in patients (age, comorbidities), type of AF (paroxysmal, persistent), anatomy (LA size, LVEF), and ablation techniques used (circumferential PVI, linear ablation, targeting complex fractionated atrial electrograms [CFAE]), but also how we define “success.” Success can be freedom from all AF off AADs, control of symptoms on AADs that previously failed, or simply reduced symptomatic AF episodes and/or duration of AF episodes. There is also the factor of how closely patients are followed postprocedure and how meticulous physicians are when monitoring for asymptomatic episodes to confirm success. In addition, the number of procedures to achieve success varies between studies. The recent Heart Rhythm Society Task Force consensus paper hopes to make the design of such a study possible by giving clear guidelines and recommendations regarding patient selection, procedural considerations, definitions of success, and follow-up.¹³

How we classify AF impacts procedural techniques and outcomes. Paroxysmal AF is defined as episodes that are self-sustained and lasting < 7 days. Persistent AF lasts > 7 days, or requires either pharmacologic or electrical cardioversion. Also within this definition is longstanding persistent AF, which is AF > 1 year in duration. Permanent AF is when cardioversion has failed or has not been attempted. The term *permanent AF* is not usually used with regard to patients being considered for AF ablation because in these patients the decision has already been made not to intervene.^{2,13}

Mechanisms of AF and Ablation Techniques

The development of AF requires a rapidly firing focus, a trigger, and a

heterogeneous anatomic substrate for both initiation and maintenance of AF. The cardiac autonomic nervous system facilitates trigger firing from the pulmonary veins (PVs). These focal triggers can cause multiple reentrant wavelets, or AF drivers, that form continuous waves of conduction that undergo wave break, which leads to fibrillatory activity.^{13,14} When high-frequency AF continues for a prolonged period of

AF is not sustainable. Electrical isolation of the PVs with circumferential lesions around PV ostia is the mainstay of AF ablation today. The PVs are the most common sites of triggers for AF, and ablation here isolates them from being able to influence LA activity.²² Additionally, the wide circumferential lesions may also alter the arrhythmogenic substrate by reducing excitable LA mass, eliminating the tissue at the atrial-PV

When high-frequency AF continues for a prolonged period of time, remodeling of the electrophysiologic properties occurs.

time, remodeling of the electrophysiologic properties occurs. This includes changes to ion channels that can lead to increased firing from foci, changes in gene expression, and fibrosis. All of these changes then contribute to the perpetuation of AF.^{15,16} Other factors that may contribute to perpetuation of AF include slowed atrial conduction velocity, shortened refractory periods, and increased atrial mass, all of which often occur as part of the final common pathway in heart disease. Spatial dispersion of refractoriness from hypertrophy, remodeling, fibrosis, and scarring further promotes reentry by conduction block and conduction delay.^{13,17}

More than 15 years ago, Haïssaguerre and colleagues¹⁸ first showed that PV ablation can provide a cure for AF in a specific subset of patients with AF by elimination of the trigger alone. These triggers are often found at the os of PVs or near the superior vena cava, where muscle sleeves are known to be present.^{19,20} These muscle sleeves are extensions of myocardial muscle fibers that are an important source of focal firing and may even have pacemaker-like automaticity.²¹

AF ablation procedures aim to eliminate the trigger and/or modify the substrate so that maintenance of

junction that often provides the substrate for reentrant circuits, as well as interrupting autonomic innervation (Figure 3).^{13,23,24} Although the cornerstone of current ablation remains the targeting of the PV antrum with complete electrical isolation of the PVs, identification of focal triggers outside the PVs can also be seen in as many as one-third of patients. Additionally, other triggering mechanisms such as atrioventricular nodal reentry tachycardia and accessory pathway are also found in a small percentage of patients and should be targeted.²⁵

A patient-specific and mechanism-guided approach is reasonable to eliminate AF with the least amount of ablation necessary and to minimize complications. For patients with paroxysmal AF the endpoint is the inability to induce AF. The initial procedural aim is at PVI when the PVs are thought to be the triggers. In those with persistent AF, a stepwise approach has shown success with conversion of AF to either NSR or atrial tachycardia; PVI alone may not be sufficient in these patients.²³ Further ablation would then call for additional linear lesion sets borrowed from surgical ablation techniques, which aim to decrease the critical mass necessary to sustain reentry. Some operators will

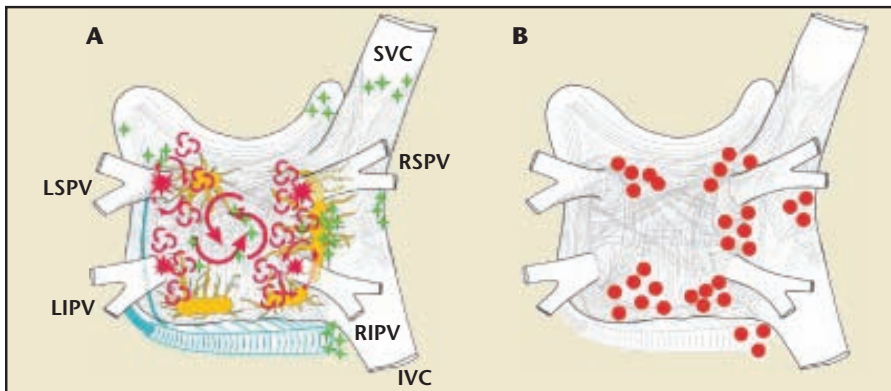


Figure 3. (A) Schematic drawing of left and right atria as viewed from the posterior. The extensions of the muscular fibers onto the pulmonary veins (PVs) can be appreciated. A composite of the anatomic and arrhythmic mechanisms of atrial fibrillation (AF): the 4 major autonomic plexi (yellow) can be seen, the coronary sinus enveloped by muscular fibers connecting to the atria (blue), reentrant wavelets (red), and common sites of non-PV triggers (green). (B) Schematic of common lesion sets used in AF ablation, such as circumferential ablation lesions around the right and left PVs, some of the most common sites of linear ablation including a roof line connecting the lesions encircling the left and right PVs, a mitral isthmus line connecting the mitral valve and the left inferior PV line, and an anterior linear lesion connecting either the roof line or the left or right circumferential lesions to the mitral annulus anteriorly. Additionally, lesion sets can also be made at sites of complex fractionated electrograms distributed throughout the left and right atria. IVC, inferior vena cava; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; SVC, superior vena cava. Reprinted from Heart Rhythm, Vol 4, Calkins H et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation, pages 816-858, copyright © 2007, with permission from Elsevier.

also target CFAE found throughout the atria, which are thought to represent AF substrate sites.²⁶

Indications for Catheter Ablation of AF

According to American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology 2006 guidelines, catheter ablation of AF is recommended for those with symptomatic AF refractory or intolerant to at least one Class 1 or Class 3 antiarrhythmic medications.² Additionally, catheter ablation of AF may be appropriate as first-line therapy in certain clinical situations and in selected symptomatic patients with heart failure and/or reduced EF. When considering the selection of appropriate patients for AF ablation one must consider that there is a lower success rate in older patients, those with increased LA size and/or volume, and those with long-term, persistent AF. A recent study looked at 73 patients undergoing AF ablation. LA size was

calculated using computed tomography (CT); mean LA volume was 119 mL in those with recurrent AF versus 98 mL for those without recurrence, and a cut-off value of 135 mL yielded a 36% sensitivity and 96% specificity for recurrence. Recurrence was determined by electrocardiograms and patients' symptoms.²⁷ Elderly patients have a higher risk for thromboembolic complications and myocardial perforation, but may actually benefit

therapy is their desire to discontinue anticoagulation treatment. There is currently a small study that showed that it may be safe to discontinue warfarin in some subsets of patients, but a large, prospective, randomized trial remains to be performed. In the study by Oral and colleagues²⁴ 755 consecutive patients had AF ablation, 490 were paroxysmal, and 265 were chronic; 56% of these patients had ≥ 1 risk factor for stroke. All were anticoagulated with warfarin for ≥ 3 months after ablation and those older than 65 years or with a history of stroke were more likely to remain on long-term anticoagulation. Thromboembolism occurred in 1.1%, with most events occurring within 2 weeks after the procedure. The authors concluded that discontinuation of anticoagulation therapy may be safe after ablation in patients without risk factors or those with risk factors other than stroke and age > 65 years.²⁴

Currently, recommendations regarding anticoagulation follow the CHAD2 criteria (Congestive heart failure, Hypertension, Age > 75 years, Diabetes, and 2 points for cerebral ischemia) (Table 1). These criteria were established based on a retrospective study looking at the stroke risk in patients with nonrheumatic AF and de-

Elderly patients have a higher risk for thromboembolic complications and myocardial perforation, but may actually benefit the most because of associated comorbidities such as intolerance to medications, heart failure, and bleeding complications secondary to chronic anticoagulation.

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Anticoagulation

Probably the biggest reason asymptomatic patients seek AF ablation

terminated that those with a CHAD2 score ≥ 2 were moderate or high risk (adjusted average annual stroke rate ≥ 4.0) and warranted anticoagulation with warfarin. Lower-risk patients (2.8 stroke rate) with a score of 1 can be treated with either aspirin or warfarin, and in those with scores of 0 (1.9 stroke rate) aspirin alone is sufficient.^{2,28}

Table 1
Components of CHAD2

CHAD2 Item		Points
Congestive heart failure		1
Hypertension (systolic > 160 mm Hg)		1
Age > 75 years		1
Diabetes		1
Prior cerebral ischemia		2

CHAD2 Score	Patients (N)	Strokes (N)	Adjusted Annual Stroke Rate (95% CI)
0	120	2	1.9 (1.2-3.0)
1	463	17	2.8 (2.0-3.8)
2	523	23	4.0 (3.1-5.1)
3	337	25	5.9 (4.6-7.3)
4	220	19	8.5 (6.3-11.1)
5	65	6	12.5 (8.2-17.5)
6	5	2	18.2 (10.5-27.4)

CHAD2, C = congestive heart failure, H = hypertension, A = age, D = diabetes, and 2 for cerebral ischemia (worth 2 points); CI, confidence interval. Adapted with permission from Gage BF et al. *JAMA*. 2001;285:2864-2870. Copyright © 2001 American Medical Association. All rights reserved.

AFFIRM showed that as many as 12% of patients have asymptomatic episodes of AF, and 57% of the strokes occurred in the rhythm control arm when patients stopped taking warfarin. Additionally, depending on how rigorous the follow-up is, this rate can be as high as 17% for episodes lasting > 48 hours.²⁹ It is therefore not recommended to discontinue warfarin therapy in those patients with a CHAD2 score ≥ 2 (moderate-to-high risk). Additionally, current postablation patients have deliberate areas of fibrosis induced by ablation, electrical discontinuity, and possible atrial standstill from extensive ablation and may actually represent a higher-risk population than those characterized by the CHAD2 classifications.¹³ Further studies in this subset are still needed and cessation of anticoagulation must be individualized for each patient.

Success of AF Ablation

The techniques for AF ablation are evolving extremely rapidly and the results of NSR maintenance must be viewed in the context of the heterogeneity of AF. AF ablation does offer patients an alternative to AADs, given their side effects and limited efficacy, and despite considerable variability, the results of catheter ablation of AF are surprisingly similar among different centers.¹² Current data on the success of the procedure are summarized in the consensus statement and are derived from single-center published trials that include more than 50 patients, 5 randomized clinical trials, and a large worldwide physician survey that details almost 9000 patients.

From the nonrandomized clinical trials in this consensus statement, success of paroxysmal AF after a single procedure is > 60%, whereas

success for persistent AF is $\leq 30\%$. Repeat procedures resulted in higher success rates with > 70% in paroxysmal AF patients and > 50% in those with persistent AF. The randomized trials compared catheter ablation of AF in either paroxysmal and/or persistent AF, primarily with AADs, and in one trial with cardioversion. The results of 1-year freedom from AF ranged from 56% to 87%.¹³ The worldwide survey shows freedom from AF following ablation off AADs was 52%, and an additional 24% of patients were free from symptoms in the presence of previously ineffective AADs. More than one procedure was performed in 27% of patients.³⁰

Most recently the first meta-analysis of radiofrequency ablation (RFA) and AAD treatment of AF was published by Calkins and colleagues.³¹ The single procedure success rate in RFA in patients off AAD therapy was 57%, and after multiple procedures this increased to 71%, which is very close to what has been reported in several recent individual randomized trials. Those patients who remained on AADs who previously may have been deemed unsuccessful had success rates of 71% and 77% for single and multiple RFA procedures, respectively. In comparison, overall efficacy for AADs was 52%, with amiodarone having the greatest efficacy over placebo.

Early recurrence of AF is common in almost 50% of patients within the first 2 months following ablation, and in 15% may even be more frequent than preablation. However, up to 60% of these patients will not have any further arrhythmias during long-term follow-up.^{32,33} Although the mechanism of early recurrence has not been proven, some of the proposed hypotheses include transient inflammation from ablation with stimulatory effects, temporary imbalance of the autonomic nervous

system causing increased trigger firing, and a delayed effect of RFA.^{13,34} Early recurrence is most commonly treated with AADs and observation. Repeat ablation is only recommended after evidence of failure occurs after 3 months or highly symptomatic atrial arrhythmias are uncontrollable with AAD therapy. Persistent, regular atrial tachycardias make up 10% of early recurrences and may often be refractory to medications. Although they also often spontaneously resolve, a second procedure may be necessary and is successful in about 90% of patients.¹³ Recurrence of arrhythmia within 1 year leads to repeat ablation procedures in 20% to 40% of patients and is more common in those with larger LA size and AF of longer duration.²⁶ Late recurrence more than 12 months after ablation occurs in 5% to 10% of patients.³⁵

Postablation AADs can be continued during the initial observational period; some advocate their use during the initial phases after ablation because the mechanism of post-ablation AF (which may spontaneously resolve) may be different than the patient's clinical arrhythmia.

Minimizing Risk and Limiting Complications

The decision to undergo AF ablation should not be made hastily as the

times for these complex ablations. When patients do elect to undergo ablation procedures, certain adjunctive tools provide increased accuracy, improved success, and minimized complications. Most centers use 3-dimensional mapping systems that can integrate magnetic resonance (MR) and CT images, which reduces fluoroscopy time and allows for creation of contiguous lesions. Imaging prior to these procedures aids in understanding anatomic relationships, variability of PV number and morphology, and increases intraprocedural accuracy.¹³ Intracardiac echocardiography (ICE) provides real-time anatomic images, confirms location of ablation lesions, and guides transseptal punctures to decrease complications of transseptal access. ICE also can be used to identify thrombus formation during the procedure, allowing for earlier intervention and prevention of thromboembolic events.¹³ Additionally, ablation catheter design is constantly evolving to improve safety with adjustments such as irrigated tips to minimize char formation, multiple electrodes to decrease procedure time with delivery of multiple simultaneous lesion sets, and the use of other energy sources such as cryoablation.

At least one major complication—defined as a complication resulting in

major complications and a total mortality of 0.7%.³¹

Common complications include the following^{14,30,31}:

- Thromboembolism (0%-7%): This typically occurs within 24 hours, but the high-risk period includes the first 2 weeks following ablation. Possible sources include disruption of already-present thrombus within the LA, development of new thrombi on LA catheters, inadequate anticoagulation intraprocedurally, and char formation on ablation catheter tips and tissue. Anticoagulation during the procedure minimizes stroke risk with maintenance of activated clotting times (ACT) > 300 seconds, which are measured every 30 minutes during the procedure. After cessation of the procedure, anticoagulation is reinitiated within 4 to 6 hours with enoxaparin (0.5 mg/kg twice daily) and warfarin. Enoxaparin is continued until a therapeutic International Normalized Ratio is achieved. Warfarin is recommended for at least 2 months after ablation.
- PV stenosis (1.3%-1.6%): From thermal injury to PV musculature; incidence has decreased significantly due to increased awareness, improved technique, and avoidance of ablation within PVs. Some physicians repeat imaging 6 months after ablation for screening, whereas others wait for symptoms and have a low threshold for further evaluation. It is unknown if early diagnosis and treatment provides any long-term benefit. Diagnosis can be made with CT/MR; symptoms include chest pain, dyspnea, cough, hemoptysis, recurrent pneumonia, and pulmonary hypertension, but can be asymptomatic even in severe forms. PV angioplasty can be performed with or without stenting.
- Cardiac tamponade or pericardial effusion (1.2%): This is managed with

The decision to undergo AF ablation should not be made hastily as the only proven benefit at this time is improvement of symptoms, and as with any procedure the possibility of complications exists.

only proven benefit at this time is improvement of symptoms, and as with any procedure the possibility of complications exists. Operator experience with specific long-term training in AF ablation and the performance of multiple previous AF ablations not only decrease complications but also minimize procedure

permanent injury or death, requiring intervention for treatment, or prolonging or requiring hospitalization—was seen in 6% of patients in the physician worldwide survey encompassing almost 9000 AF ablation procedures (Table 2). The recently published meta-analysis corroborates the survey data, showing a rate of 5% for

Table 2
Major Complications

Complication Type	Patients (N)	Patients (%)
For all types of procedures (n = 8745)		
Periprocedural death	4	0.05
Tamponade	107	1.22
Sepsis, abscesses, or endocarditis	1	0.01
Pneumothorax	2	0.02
Hemothorax	14	0.16
Permanent diaphragmatic paralysis	10	0.11
Femoral pseudoaneurysm	47	0.53
Arteriovenous fistulae	37	0.42
Valve damage	1	0.01
Aortic dissection	3	0.03
For procedures involving left atrial ablation (n = 7154)		
Stroke	20	0.28
Transient ischemic attack	47	0.66
Pulmonary vein stenosis		
No. with > 50% stenosis		
Acute	23	0.32
Chronic	94	1.31
No. with closure		
Acute	2	0.03
Chronic	15	0.21
Patients with symptoms		
Acute	3	0.04
Chronic	41	0.57
Patients undergoing intervention		
Percutaneous	51	0.71
Surgical	2	0.03
Grand total	524	5.9

Adapted with permission from Cappato R, Calkins H, Chen SA, et al. Worldwide survey on the methods, efficacy and safety of catheter ablation for human atrial fibrillation. *Circulation*. 2005;111(9):1100-1105.

immediate pericardiocentesis and reversal of anticoagulation with protamine. Rarely, this may require surgical repair.

- Phrenic nerve injury (< 0.5%): The right phrenic nerve is located near the right superior PV, more commonly seen with balloon ablation catheters. Symptoms include dyspnea, hiccups, atelectasis, pleural effusion, cough, and thoracic pain. Phrenic nerve function usually recovers within 12 months, but there

have been a few case reports of permanent injury and there is no treatment to aid healing.

- Esophageal injury and atrioesophageal fistula (< 0.25%): This is one of most serious complications because of the high mortality. This typically presents 2 to 4 weeks after ablation with fever, chills, and recurrent neurologic events. If suspected, the best diagnostic tool is CT/MR. Endoscopy should be avoided as insufflation of air in the esophagus can

result in massive cerebrovascular accidents and death from air emboli.

AADs in the meta-analysis showed a 30% rate of major complications with an overall mortality of 2.8%. This makes the rate of RFA complications appear to have a much lower risk. One must remember, though, that the complications from RFA tend to be more serious, whereas the most common complications from AADs include gastrointestinal upset, neuropathy, and thyroid dysfunction.³¹

Monitoring

Early recurrences of AF are common and therefore the first 3 months postprocedure serve as a blanking period where return of atrial arrhythmia is not considered true recurrence or procedural failure. Efficacy assessment and repeat procedures should be delayed until after this time period.

After the first 3 months asymptomatic AF frequently occurs in ablation patients; the longer the patient is monitored, the better the likelihood of detecting AF. Patients should at least have 24-hour Holter monitoring at 3- to 6-month intervals for 1 to 2 years after ablation to screen for asymptomatic episodes, especially if termination of anticoagulation is considered.¹³

Surgical Options for AF Ablation

Surgical AF ablation has also evolved over the past 20 years; indications for surgical AF ablation include those undergoing other cardiac surgery as well as those who prefer a surgical approach, have failed catheter ablation, or those who are not candidates for catheter ablation.² The cut-and-sew Cox-Maze III procedure includes making strategically placed incisions across both the right and left atria in addition to isolating the PVs, posterior LA, and amputation of the left

atrial appendage. This successfully restores AV synchrony and decreases the incidence of stroke. Late follow-up shows 90% of patients are free of symptomatic AF at 1 year. Current ablative technologies have mostly replaced the cut-and-sew method. Various recent retrospective studies looking at the ablation Cox-Maze procedure showed success rates between 65% and 95% at 6 months. This variability is largely due to physician experience, the precise lesion sets made (PVI, LA lesions, full Cox-Maze biatrial lesions), the use of different ablation technologies (unipolar-cryosurgery, radio frequency, ultrasound, laser, or bipolar clamps), as well as all the other variables seen for catheter ablation. Similar determinants of failure also exist, such as duration of AF, LA size, and advanced patient age.¹³

All patients with AF undergoing other cardiac surgery should be considered for surgical AF ablation because the additional risk is low and there is a reasonable success rate. Stand-alone surgery for using ablation technology and less invasive techniques have been reported in small

series and have limited follow-up.¹³ As with catheter ablation, large prospective multicenter clinical trials are still needed to define success rates and assess safety and efficacy. There have also been no randomized studies performed comparing the stand-alone surgical treatment with catheter ablation. Therefore, the decision to recommend surgical or interventional ablation for AF should be based on physicians' expertise, individualized risks, and patient preference.

Conclusions

AF ablation has changed significantly in the past several years and the number of patients seeking an interventional alternative is grow-

ing. Further developments include multiple new technologies mostly for delivery of contiguous lesion sets to PV ostia targeting PV triggers. These include balloon-based ablation systems such as high-intensity, focused ultrasound and cryoablation, as well as customized circular RFA catheters. All of these aim to shorten procedure time and improve efficacy. The use of robotic systems for navigation may further improve accuracy while minimizing fluoroscopy exposure for both patients and physicians.³⁶

The discovery of the underlying mechanisms have allowed for the evolution of new techniques and the identification of specific targets. Currently, efficacy is best for minimizing the symptoms of AF and improving QoL. There is also growing evidence that patients in sinus rhythm have a better prognosis. Suppression of symptomatic AF can be achieved

Suppression of symptomatic AF can be achieved through catheter ablation in approximately 70% of patients.

ing. Further developments include multiple new technologies mostly for delivery of contiguous lesion sets to PV ostia targeting PV triggers. These include balloon-based ablation systems such as high-intensity,

through catheter ablation in approximately 70% of patients. Although it is possible to achieve symptomatic control, studies have yet to show a mortality benefit or even a reduction in stroke risk. What we do know is

Main Points

- Atrial fibrillation (AF) contributes to considerable morbidity, with increasing risk of stroke, complications from anticoagulation, and exacerbation of heart failure. Due to multiple contraindications, many patients with AF are not candidates for antiarrhythmic drugs (AADs). Catheter-based ablation of AF offers patients the benefit of mortality reduction but without the resultant side effects of AADs.
- The cornerstone of current ablation therapy remains the targeting of the pulmonary vein (PV) atrium with complete isolation of the PVs.
- According to recent guidelines, catheter ablation of AF is recommended for those with symptomatic AF refractory or intolerant to at least one Class 1 or Class 3 antiarrhythmic medications; additionally, it may be appropriate as first-line therapy in selected symptomatic patients with heart failure and/or reduced ejection fraction. Suppression of symptomatic AF can be achieved in approximately 70% of patients.
- Discontinuation of anticoagulation therapy may be safe after ablation in patients without risk factors or those with risk factors other than stroke and advanced age.
- Complications of AF ablation may include thromboembolism, PV stenosis, cardiac tamponade, phrenic nerve injury, and esophageal injury.
- Patients should have Holter monitoring at 3- to 6-month intervals for 1 to 2 years following ablation, especially if discontinuation of AADs is considered.

that AF begets AF, and those with truly paroxysmal episodes have better success rates than those with longstanding persistent AF.

It is possible that further studies will show that the return to sinus rhythm with AF ablation can positively influence remodeling and inhibit the progression of disease; therefore, it can become a first-line, safe option for an even greater portion of the AF population. For now, AF ablation is a viable option as an alternative to medical management for patients who are highly symptomatic, have failed AAD treatment, have structurally normal hearts, are younger, and have paroxysmal episodes that are self-limited. Cardiologists and electrophysiologists must work together in the management of these patients with close follow-up for monitoring of recurrences and possible complications. ■

References

- Feinberg WM, Blackshear JL, Laupacis A, et al. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med*. 1995;155:469-473.
- Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e257-e354.
- Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA*. 2005;293:2634-2640.
- Hsu LE, Jais P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. *N Engl J Med*. 2004;351:2373-2383.
- Pappone C, Oreto G, Rosanio S, et al. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: efficacy of an anatomical approach in a large cohort of patients with atrial fibrillation. *Circulation*. 2001;104:2539-2544.
- Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med*. 2002;113:359-364.
- Corley SD, Epstein AE, DiMarco JP, et al. Relationships between sinus rhythm, treatment, and survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AF-FIRM) Study. *Circulation*. 2004;109:1509-1513.
- Pedersen OD, Bagger H, Keller N, et al. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function. A Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND) Substudy. *Circulation*. 2001;104:292-296.
- Pappone C, Rosanio S, Augello G, et al. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation. *J Am Coll Cardiol*. 2003;42:185-197.
- Heart Rhythm 2006. Abstracts of the 27th Annual Meeting of the Heart Rhythm Society, Boston, Massachusetts, USA, May 17-20, 2006. *Heart Rhythm*. 2006;3(1 suppl):S1-S460.
- Pappone C, Augello G, Sala S, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF study. *J Am Coll Cardiol*. 2006;48:2340-2347.
- d'Avila A, Ruskin J. Nonpharmacologic strategies: the evolving story of ablation and hybrid therapy. *Am J Cardiol*. 2008;102:20H-24H.
- Calkins H, Brugada J, Packer D, et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. 2007;4:816-858.
- Patterson E, Po SS, Scherlag BJ, Lazzara R. Triggered firing in pulmonary veins initiated by in vitro autonomic nerve stimulation. *Heart Rhythm*. 2005;2:624-631.
- Allesie M, Ausma J, Schotten U. Electrical, contractile, and structural remodeling during atrial fibrillation. *Cardiovasc Res*. 2002;54:230-246.
- Everett TH 4th, Wilson EE, Verheule S, et al. Structural atrial remodeling alters the substrate and spatiotemporal organization of atrial fibrillation: a comparison in canine models of structural and electrical atrial remodeling. *Am J Physiol Heart Circ Physiol*. 2006;291:H2911-H2923.
- Allesie MA, Lammers WJEP, Bonke FIM, Hollen J. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation. In: Zipes DP, Jalife J, eds. *Cardiac Electrophysiology and Arrhythmias*. New York: Grune & Stratton; 1985.
- Haissaguerre M, Marcus FI, Fischer B, Clémenty J. Radiofrequency catheter ablation in unusual mechanism of atrial fibrillation: report of three cases. *J Cardiovasc Electrophysiol*. 1994;5:743-751.
- Jais P, Haissaguerre M, Shah DC, et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation*. 1997;95:572-576.
- 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;339:659-666.
- Perez-Lugones A, McMahon JT, Ratliff NB, et al. Evidence of specialized conduction cells in human pulmonary veins of patients with atrial fibrillation. *J Cardiovasc Electrophysiol*. 2003;14:803-809.
- Ouyang F, Bänsch D, Ernst S, et al. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. *Circulation*. 2004;110:2090-2096.
- Haissaguerre M, Sanders P, Hocini M, et al. Catheter ablation of long-lasting persistent atrial fibrillation: critical structures for termination. *J Cardiovasc Electrophysiol*. 2005;16:1125-1137.
- Oral H, Chugh A, Ozaydin M, et al. Risk of thromboembolic events after percutaneous left atrial radiofrequency ablation of atrial fibrillation. *Circulation*. 2006;114:759-765.
- Chen SA, Tai CT. Catheter ablation of atrial fibrillation originating from the non-pulmonary vein foci. *J Cardiovasc Electrophysiol*. 2005;16:229-232.
- Nademanee K, McKenzie J, Kosar E, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol*. 2004;43:2044-2053.
- Helms AS, West JJ, Patel A, et al. Relation of left atrial volume from three-dimensional computed tomography to atrial fibrillation recurrence following ablation. *Am J Cardiol*. 2009;103:989-993.
- Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke. Results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285:2864-2870.
- Kaufman ES, Waldo AL. The impact of asymptomatic atrial fibrillation. *J Am Coll Cardiol*. 2004;43:53-54.
- Cappato R, Calkins H, Chen SA, et al. Worldwide survey on the methods, efficacy and safety of catheter ablation for human atrial fibrillation. *Circulation*. 2005;111:1100-1105.
- Calkins H, Reynolds M, Spector P, et al. Treatment of atrial fibrillation with anti-arrhythmic drugs or radio-frequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhythm Electrophysiol*. 2009;2:349-361.
- Oral H, Knight BP, Ozaydin M, et al. Clinical significance of early recurrences of atrial fibrillation after pulmonary vein isolation. *J Am Coll Cardiol*. 2002;40:100-104.
- O'Donnell D, Furniss SS, Dunuwille A, Bourke JP. Delayed cure despite early recurrence after pulmonary vein isolation for atrial fibrillation. *Am J Cardiol*. 2003;91:83-85.
- Kobza R, Hindricks G, Tanner H, et al. Late recurrence of arrhythmias after ablation of atrial fibrillation: incidence, mechanisms, and treatment. *Heart Rhythm*. 2004;1:676-683.
- Mainigi SK, Sauer WH, Cooper JM, et al. Incidence and predictors of very late recurrence of atrial fibrillation after ablation. *J Cardiovasc Electrophysiol*. 2007;18:69-74.
- Spragg D, Calkins H. Catheter ablation for AF: past, present, and future. *J Atr Fibrillation*. 2008;1:221-229.