

Invasive Management of Atrial Fibrillation and the Elderly

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered by caregivers for the elderly. A plethora of new, mostly invasive techniques have evolved to treat patients who remain symptomatic from this arrhythmia despite attempts at pharmacological therapy.¹⁻⁴ The most widely-used of these new techniques is radiofrequency ablation, but in selected patients, special types of pacemaker, cryoablation, and surgical maze therapy may be of benefit.

In this article, we review the significance of these new techniques for the elderly population. After a brief summary of the relevant epidemiological and pathological bases for classifying AF and the basis for clinical decision-making in terms of who is likely to benefit most from these procedures, we then provide a description of the techniques, anticipated success rates, and complications associated with AF ablation to guide the primary caregiver in counseling patients with symptomatic AF. Because of the relative novelty of ablation in the elderly and very elderly, risk benefit analysis when counseling these patients can be challenging. Reports assessing ablation for AF in the geriatric population have recently become available.⁵⁻⁸ A brief overview of non-ablation invasive management strategies, including pacemakers, defibrillators, and the surgical maze procedure is then included.

The evidence for PV isolation

Approximately five million patients in the United States have AF, and this number is expected to double to 10 million over the next 30 years.⁹ Being a signature disease of the elderly, it has a prevalence of about 5% in people aged 65 years and older and affects approximately 10% of those 80 years old.¹⁰ Current estimates state that by the year 2050, 12 to 15 million people in the United States will be affected by AF. This is not surprising since the ATRIA trial (2001) found that beginning at 50, the prevalence of AF almost doubles with each decade of life; increasing from 0.5% at age 50 to 59 years to 5% to 7% or greater in those aged 70 to 79 years. Even more relevant, the Framingham Heart Study found that the arrhythmia may be an independent risk factor for death with a relative risk of about 1.5 for men and 1.9 for women after adjustment for known risk factors.

Although aging is the major risk factor for developing AF, other reversible factors must be ruled out before targeting age alone as the culprit, e.g. myocardial infarction, valvular disorders, status post cardiac surgery, pericarditis, alcohol use ("holiday heart"), pneumonia, pulmonary embolism, hyperthyroidism, structural, caffeine, pheochromocytoma, chest tumor, stroke, and other forms of SVT in the setting of Wolff-Parkinson-White Syndrome.

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The current guidelines for managing AF focus on control of heart rate and rhythm, along with prevention of thromboembolism. Non-valvular AF increases the risk of ischemic stroke by approximately five-fold and causes an estimated 15% of all strokes in the United States. In people 80 to 89 years old, this proportion is even higher, approximately 24%.¹⁰ Oral anticoagulants are highly effective in preventing AF-related stroke, but since the oldest patients are likely to have the highest risk for hemorrhage on warfarin, prescribing anticoagulation is a dilemma that clinicians face, especially for the geriatric population.⁷⁻⁸

Another matter of contention is the issue of rate-control versus rhythm-control. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial pitted these treatment strategies against each other, only to find no significant difference in mortality. Additionally, symptom management and the need for pharmacologic therapy are being increasingly challenged with invasive electrophysiologic techniques that abolish the need for drugs and rid patients of symptoms.

Classification

The term "lone atrial fibrillation" has been used

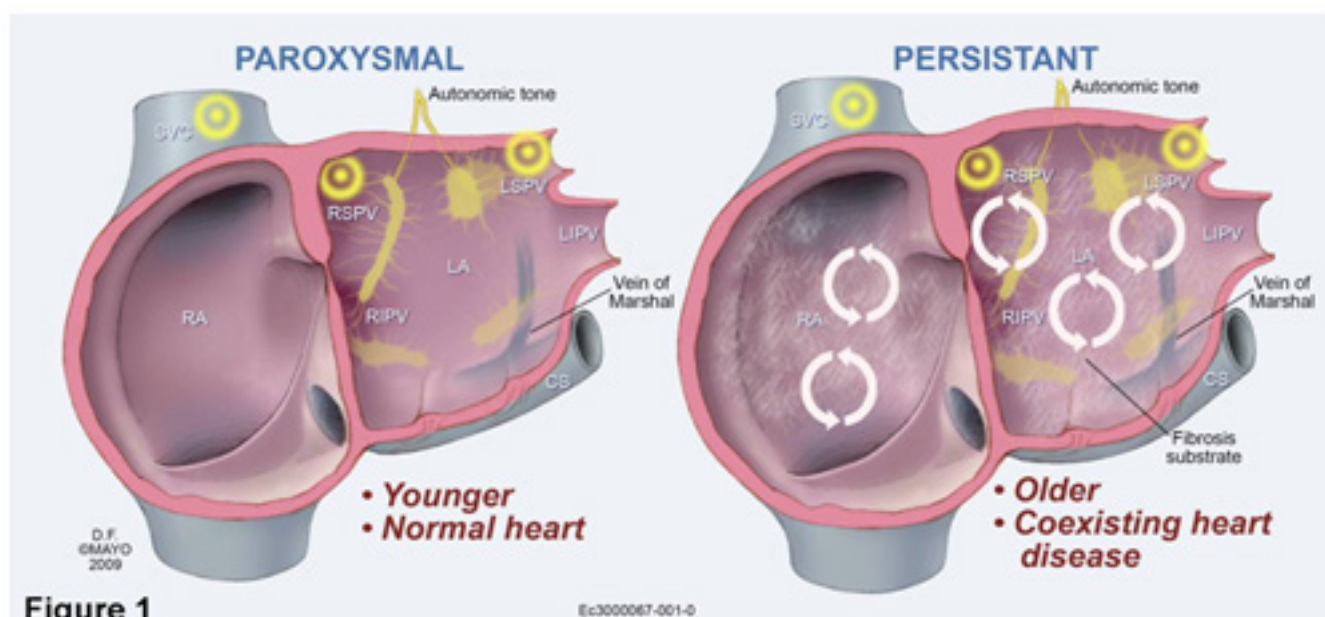
Figure 1: Illustration of the two types of atrial fibrillation. Paroxysmal AF typically occurs in younger patients with normal hearts, however may be seen for the first time in the elderly and is often more symptomatic than persistent AF. Paroxysmal is often "trigger"-related with the pulmonary veins and other thoracic veins targeted for ablation when treating this type of AF. Persistent AF involves abnormalities of the atrial myocardium itself, and ablation approaches often require more than pulmonary vein isolation alone.

to describe AF that occurs in the absence of demonstrable underlying cardiac disease or history of hypertension. Lone AF occurs in approximately 3% of patients with AF. Patients with lone AF over the age of 61 have an increased risk of stroke and death.¹¹

AF may also be classified as paroxysmal AF or non-paroxysmal (chronic) AF. Paroxysmal AF may last from a few seconds to several weeks. In the strictest sense, paroxysmal AF patients experience episodes that terminate spontaneously within seven days and usually within 24 hours; 68% presenting with AF of less than 72 hours duration spontaneously converted to sinus rhythm.¹² Approximately 40% of all cases of AF are paroxysmal.¹ Non-paroxysmal, on the other hand, refers to AF that lasts longer than seven days and requires cardioversion for termination. Finally, the term permanent (or chronic) AF is used to describe AF that has been present for more than seven days and cannot be consistently terminated with cardioversion.¹³⁻¹⁵

Pathogenetic basis for invasive AF management

AF is in a sense two separate diseases rolled in one. One disease represents triggering of AF often from one of the thoracic veins, and the second disease is one of changes that occur in the atrial myo-



cardium itself that enables the persistence of AF in a given patient. Aging results in several changes in the electrophysiology of the atrium, including increases in the refractory period, prolongation of conduction times, and fibrosis, thus creating the substrate for persistent AF [Figure 1].^{11, 16-18} Hypertension, which is common in the elderly, does increase atrial and pulmonary venous stretch and may contribute to the increase in trigger-mediated AF in the elderly, as well.^{5,8}

Electrical Remodeling

Electrical remodeling occurs when repeated episodes of rapidly firing atrial foci result in marked shortening of the atrial refractory period and the loss of the normal lengthening of atrial refractoriness at slower heart rates. These rapidly firing foci are usually found in or near the pulmonary veins,¹¹ which are electrically active structures with a sleeve of syncytial myocardium that extends from the atrium into the vein.^{19,20,21} Additionally, other thoracic veins other than the pulmonary vein can serve as potential triggers. The smooth muscle that

lines these thoracic veins is electrophysiologically distinct from the endocardium proper. This venous muscle has a shorter effective refractory period and is capable of more rapid discharge than the endocardium. Additionally, myocardium has been known to extend into the vein of Marshall and into the superior vena cava, again acting as a foci for generating irregularly firing potentials. Such foci may mimic the appearance of AF on the surface electrocardiogram, or more commonly, it may degenerate into or trigger classic AF after a brief burst of ectopic activity.^{11,17,22,23}

Clinical assessment prior to invasive management

While the diagnosis of AF is usually straightforward, specific features are important to evaluate when counseling patients on the appropriateness. The clinical profile that correlates best with benefit from invasive management is the patient who has paroxysmal AF and minimal or no underlying structural heart disease. Symptoms may include palpitations, fatigue, or unexplained episodic

Figure 2: Typical electrocardiogram of AF illustrating the common reasons or symptoms seen in patients. Periods of rapid ventricular rates may give rise to palpitations, and the marked irregularity results in unpredictable ventricular filling and may result in fatigue or exertional dyspnea



shortness of breath that has been correlated with electrocardiographic documentation of AF [Figure 2].^{1, 10, 11}

General Management

While the focus of this review is invasive management strategies for the elderly patient with AF, in the next few paragraphs, we briefly outline the present guidelines for anticoagulation and for choosing between rate-control versus rhythm-control strategies in elderly patients with AF.

Anticoagulation

In the ACC/AHA/ESC Guidelines for Management of Patients with Atrial Fibrillation, patients with a CHADS2 score of 1 may be treated with either aspirin or warfarin, while patients with a CHADS2 score of 0 should receive aspirin alone. Warfarin reduces the risk of stroke by about 68% and mortality by 33%. Aspirin, on the other hand, reduces strokes by 21%. Since optimal anticoagulation occurs between International Normalized Ratios of 2.0 to 3.0, low fixed-dose warfarin has been shown to be ineffective in preventing strokes.¹⁰ For patients over 65 years who were treated with warfarin for the first time, the incidence of major hemorrhage was 13.1 per 100 person-years for patients over 80 years of age, and 4.7 for those less than 80 years old. The risk of hemorrhage was highest in patients with CHADS2 scores greater than 3, exactly the patients who would appear to be most in need of anticoagulation to prevent thromboembolism.²⁴ Current studies are underway that weigh the risks and benefits of direct, competitive thrombin inhibitors for the use of anticoagulation in AF. Dabigatran has been recently studied and shown to result in hemorrhagic stroke less often than warfarin and so may be a drug that is safe and an effective alternative to warfarin.²⁵ Further investigation is needed, however, and for now warfarin remains the most effective drug to prevent stroke in elderly patients at risk with AF.

Rate versus Rhythm

For those patients in whom no reversible cause is found for AF, a management strategy for minimizing symptoms and thromboembolic phenomenon must be chosen [Figure 3]. Rate control refers to control the ventricular rate in order to

preserve adequate hemodynamics by either pharmacologic or non-pharmacologic means. Rhythm control refers to an active attempt to keep the patient in sinus rhythm as much as possible, whether it is through the use of anti-arrhythmic drugs (e.g. amiodarone, propafenone, sotalol), DC cardioversion, percutaneous ablation, or even sometimes surgery. The AFFIRM trial compared the efficacy in regards to mortality of both management strategies and found no significant differences in mortality or quality of life in patients assigned to a rate-control strategy versus a rhythm-control strategy.

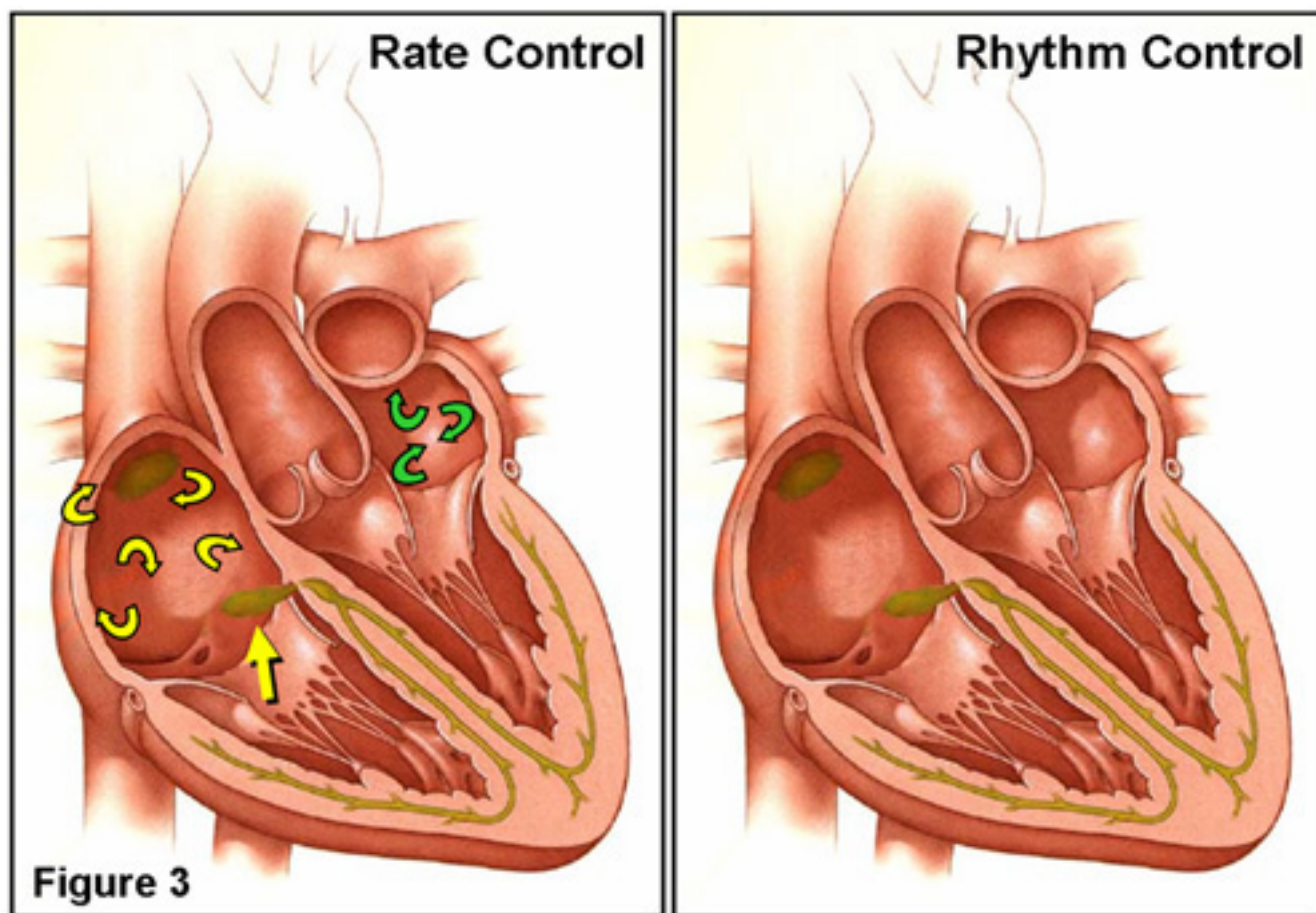
Rhythm control was associated with a statistically insignificant trend toward higher mortality, and hospital admissions were more frequent in this group. Additionally, follow-up investigations of the AFFIRM trial showed that there was modest improvement in six-minute walk distances with the rhythm-control arm and that there was no difference in cognitive function between the study arms.²⁶ The study has shown that less emphasis should be placed on the path of management and more should be placed on regaining functionality.

Elderly, minimally symptomatic patients will likely benefit greatly more from rate control rather than rhythm control, while those who are maximally symptomatic may do better with rhythm control whether by non-pharmacologic or pharmacologic means. Unfortunately, drug therapy is ineffective for long term treatment of AF with a 60% failure rate over a two-year treatment period.^{9, 27} As such, we will focus on the non-pharmacologic invasive strategies that contribute to both rate and rhythm control and discuss the success, complications, and post-procedure management.

Ablation for AF: What is it and for whom should we recommend it?

Having established that rate control with anticoagulation is a completely valid option for managing AF, we need to consider which patients we would still recommend an invasive procedure. Patients who continue to exhibit symptoms despite pharmacological therapy represent the only present indication for AF ablation. Specifically, AF ablation should not be recommended with the idea of decreasing mortality or decreasing stroke risk since there is no data to support such contentions.²⁷⁻²⁹

Figure 3: Illustration of the primary approaches to manage symptoms in patients with AF. With rate control strategies AF continues, but drugs to slow the AV node (yellow arrow) are used to minimize patients' symptoms (palpitations). With rhythm-control strategy, an attempt is made to maintain the patient in sinus rhythm. AV node ablation is an effective mean to achieve a rate control, whereas focal ablation targets rhythm control when pharmacotherapy has failed and patients remain symptomatic



Some patients remain symptomatic with palpitations because rate control is not possible or there are intolerable side effects associated with AV nodal blocking drugs. For such patients, AV node ablation and permanent pacemaker implantation should be considered. Another large group of patients have symptoms, however, including fatigue despite rate control, and they have failed pharmacological attempts to maintain sinus rhythm. For these patients, "focal" ablation targeting the triggers and possibly modifying the substrate responsible for AF may be appropriate.^{27, 29}

AV Junction Ablation and Pacemaker Placement

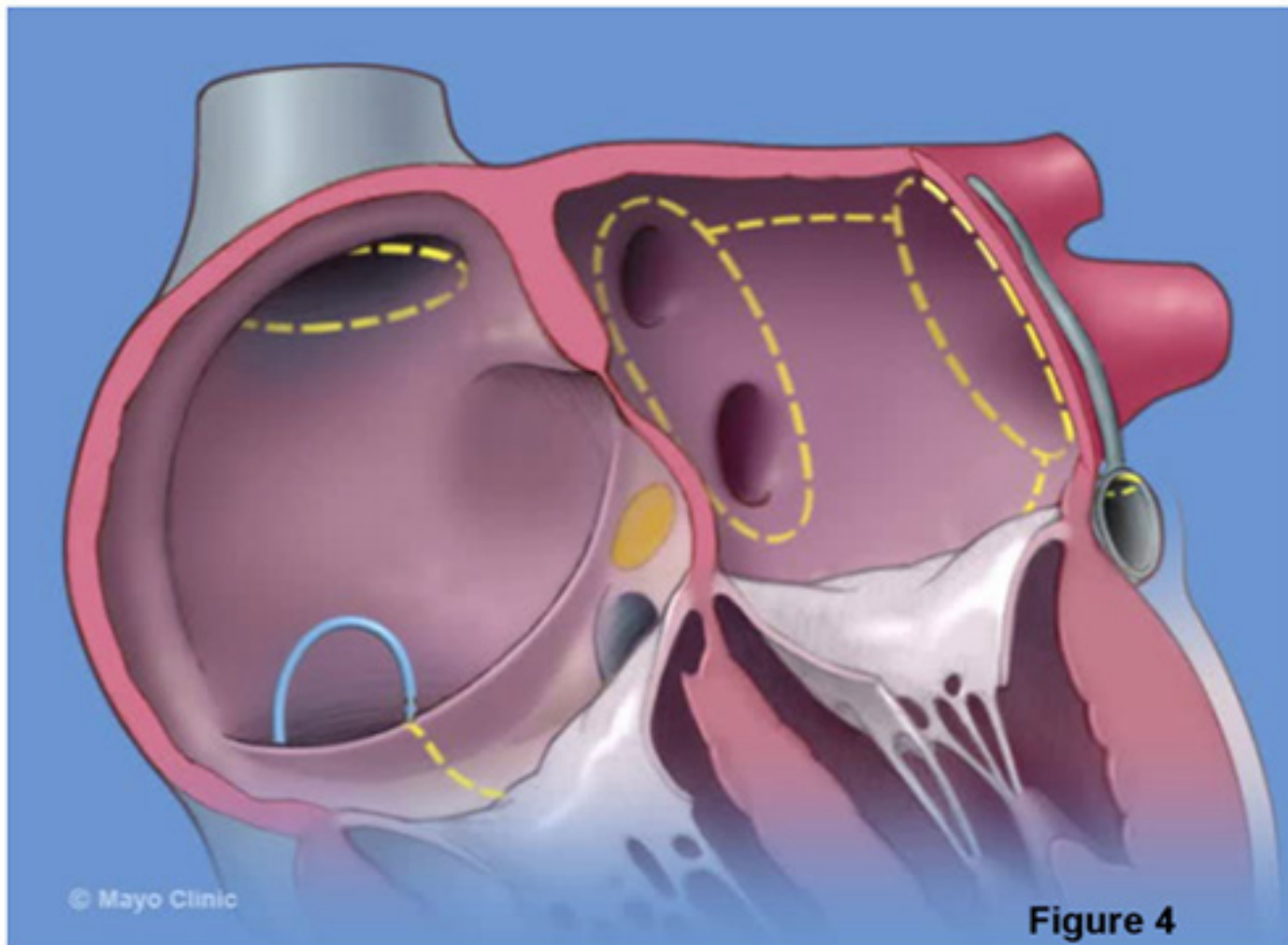
When patients do not respond to drug therapy, AV junction ablation combined with permanent pacemaker implantation can be considered. Additionally, the procedure can be used in persistent, drug-refractory AF and systolic dysfunction.^{1, 11} This procedure eliminates the posterior atrial inputs

to the AV node and essentially produces complete heart block, with a slow junctional escape rhythm, for those patients whose ventricular rate is difficult to control. With pacemaker dependence, the patient is likely to have decreased symptoms and have an improved quality of life.¹² Furthermore, control of the rapid ventricular rate has been also associated with decreased risk of the development of tachycardia-mediated cardiomyopathy.^{11, 30} Nonetheless, AV node ablation has been shown to have a neutral effect on overall survival.²⁹

Focal Ablation

Focal ablation refers to the identification and ablation of rapidly firing atrial foci located usually in the thoracic veins. During the foci isolation procedure, a mapping catheter is placed into the area of interest, and characteristic abnormal electrical findings are seen on the intracardiac tracing [Figure 4]. The foci is then ablated and

Figure 4: Illustration of the primary approaches in trigger ablation. Circumferential ablation (hatched yellow lines) is done around the pulmonary veins, as well as the superior vena cava. In addition, to address substrate abnormalities, linear ablation, both in the right and left atrium is performed



essentially electrically disconnected from the atria. The thoracic veins include the pulmonary veins, vein of Marshall, or the superior vena cava. While pulmonary vein isolation is the most common type of ablation for AF, the isolation of the thoracic veins is usually reserved for those patients who have paroxysmal AF associated with a structurally normal heart and frequent atrial ectopy.^{11, 27, 28}

In the elderly, diastolic disease, valvular dysfunction, possibly fibrotic atria, etc., all contribute to the cause of AF and require ablation of the specific atrial substrate. Substrate modification is based on the principle that ablation can 1) compartmentalize the muscle mass of the atria, containing fibrillatory spread and 2) reduce the muscle mass necessary to sustain fibrillation.^{31, 32}

Ablation targeting the thoracic veins and other triggers for AF may be insufficient in the elderly

because of these changes in the atrial substrate. More recent ablation paradigms involve attempts to modify the substrate with linear ablation in the left and right atria and in some instances targeting the retroatrial ganglionated plexuses so as to globally modify the atrial substrate.^{29, 33}

Pacemakers

Pacemakers are not a first-line or standalone therapy for AF. Nevertheless, there are some instances where pacemakers may benefit elderly patients with AF.¹²

- Some patients with AF have tachy-brady syndrome with underlying significant sinus node dysfunction. The symptoms for these patients may in fact be the bradyarrhythmia and chronotropic incompetence readily amenable to pacemaker therapy.³⁴

- As described above, following AV node ablation, permanent ventricular pacing is required.

- Special types of pacemakers called antitachycardia devices [Figure 5] may be considered in some symptomatic patients. These devices are not helpful in preventing or treating AF; however, they can be quite effective in treating atrial flutter.

- In general, pharmacological therapy with agents such as flecainide or propafenone may be reasonably effective in controlling AF but are poor in terms of preventing or treating atrial flutters. For such patients, a combined approach of pharmacological therapy and an antitachycardia pacemaker may be considered.¹²

Defibrillators

Atrial defibrillators are implanted cardiac devices that “shock” the patient automatically out of AF. These devices may be attractive in patients with rare recurrences of AF but who typically require cardioversion to minimize the surprise factor and pain associated with defibrillator therapy. The device can be programmed to administer therapy only at night or when “commanded” by the patient or physician. Despite these options, because of the discomfort with therapy and the fact that AF is not being prevented, very few patients at the

present time are treated in this fashion.³⁵⁻³⁷

Surgical Procedures: Maze and Mini-Maze

The Maze III operation is a classic ablation procedure that abolishes the macro-reentry responsible for AF.³⁸ The 15-year success rate of the Maze III operation has been reported to be as high as 97% for AF associated with other cardiac conditions. This procedure, although it is successful, is not widely adopted because of the need to perform extensive incisions and suturing of the atriums, which results in lengthy procedures with increased aortic cross-clamp times. The procedure is usually performed during other open-heart surgery, such as mitral valve replacement. The Mini-Maze procedure was developed in an effort to establish feasibility and decrease complications [Figure 6]. Multiple studies have been done using different variations of the principle developed by Dr. James Cox.³⁸ He established a lesion pattern that included encircling the pulmonary vein lesion, the left atrial isthmus with attendant coronary sinus lesion, and the right atrial isthmus lesion. High-Intensity Focused Ultrasound is currently being investigated in Europe as a potential source of epicardially-initiated ablation. It does so by causing cells to oscillate and to destroy themselves through the heat generated by friction, and may do without damaging the coronary arteries.

Figure 5: Electrocardiogram of typical atrial flutter. Antiarrhythmic agents are generally more effective for atrial fibrillation than atrial flutter. In such cases, combined approaches using membrane active drugs for AF and either ablation or antitachycardia pacemaker-based therapy for atrial flutter can be useful



Figure 6: Cartoon illustration of the principle underlying the surgical maze procedure. In the classic cut-and-sew maze procedure, suture lines are placed around the pulmonary veins, as well as in the right and left atria. The atrium is effectively compartmentalized and thus minimizing the chance of the atria fibrillating, yet the sinus node impulse is still allowed to “navigate the maze” to activate the ventricle via the AV node (see text for details)

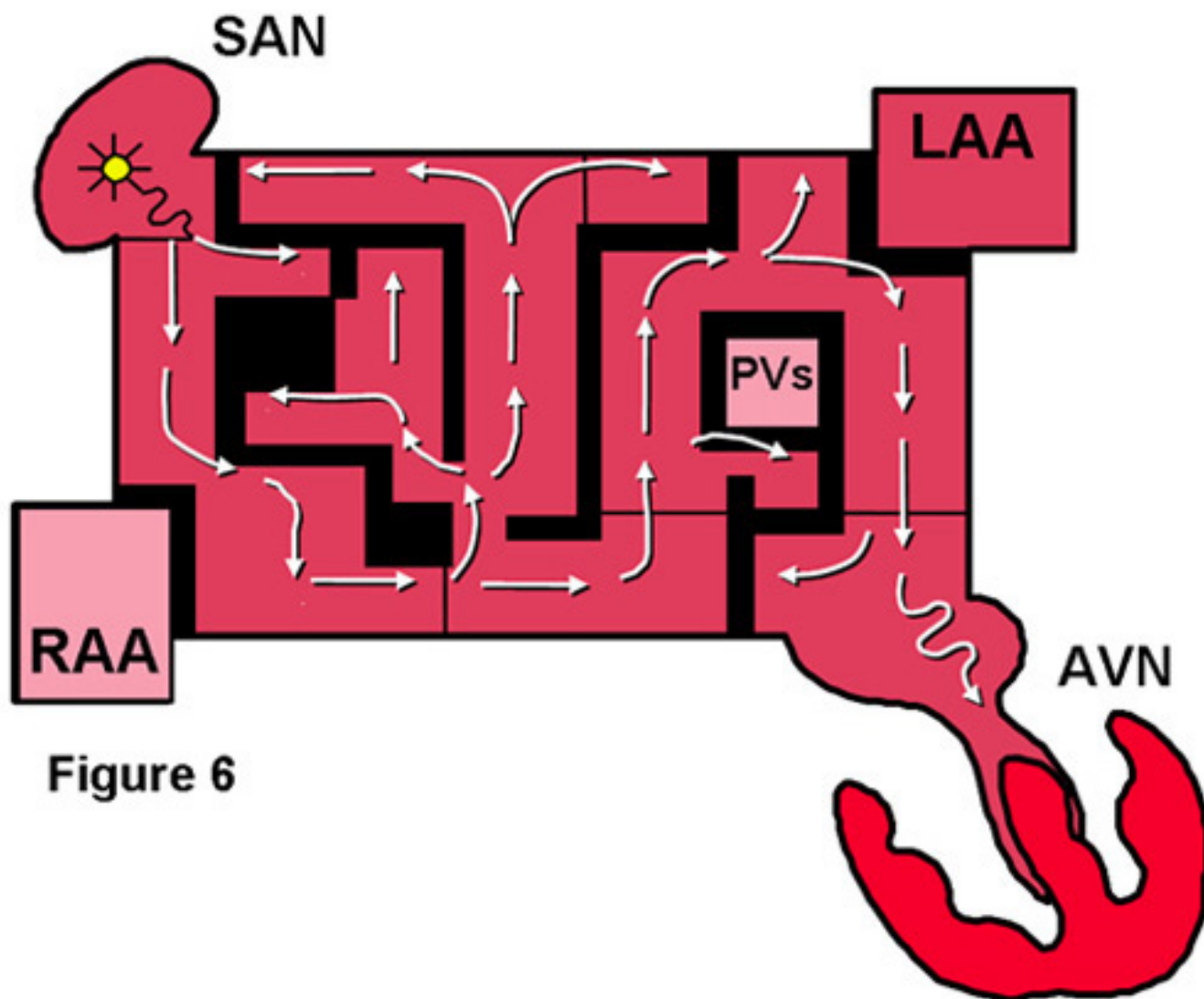


Figure 6

In summary, the classical open surgical cut-and-sew maze procedure remains the most invasive technique available to maintain sinus rhythm. However, the morbidity associated with this procedure precludes widespread use except in patients who are already having an open cardiac surgical procedure for other reasons. Newer variants of this classic procedure, including thoracoscopic and limited maze procedures appear to be less invasive. However, at present, success rates in the long term are limited.^{39, 40}

How Successful is AF ablation?

When counseling patients, it should be emphasized to them that AF ablation is not a long term

cure for AF, especially in patients with more persistent forms of this disease. Typically, 60% to 70% of patients can be expected to be symptom free with or without adjunctive antiarrhythmic therapy and with approximately 10% to 40% requiring a second ablation procedure for full benefit.^{16, 23, 41-45}

When comparing the efficacy of AV junction ablation with focal ablation [29] AV node ablation is more definitive, especially with near 100% relief from palpitation as a symptom. Nevertheless, a majority of elderly patients with paroxysmal AF may anticipate benefit with symptom-relief and without the need for permanent pacing when the focal ablation approaches described above are utilized.^{1, 9}

What are the complications with AF ablation? Are they more likely in the elderly?

Catheter ablation is generally a safe and effective procedure. However, given the invasive nature and requirement for placing electrode-tipped catheters into the heart, complications do occur.⁴⁶

Some complications are considered relatively minor and are germane to all invasive cardiac procedures, including bleeding, infection, cardiac perforation potentially requiring epicardial drainage, and vascular complications.

The more serious complications of AF ablation include stroke and TIA as a result of coagulum or thrombus formation during left atrial ablation⁴⁷ and pulmonary vein stenosis.⁴⁸ Because ablation is done near the pulmonary veins, 4% to 10% of patients may develop narrowing of the pulmonary vein. This may be asymptomatic, but some patients, particularly those with severe multivessel stenosis, may have significant shortness of breath, hemoptysis, cough, and chest pain. In these cases, percutaneous pulmonary vein angioplasty may be required to resolve symptoms.^{13, 49-53}

Another rare but potentially life-threatening complication of AF ablation involves the occurrence of left atrial esophageal fistula formation. Here, a direct fistulous connection between the left atrium and the esophagus is created. Patients may experience odynophagia, endocarditis, and air embolization producing stroke-like syndromes. Prompt recognition and surgical treatment is essential to save life.⁵⁴

The risk for these serious complications appear to be significantly reduced with present techniques to minimize energy delivery in the left atrium and the use of adjunctive imaging resources, such as intracardiac ultrasound to guide ablation therapy.⁵⁵

Although some studies have demonstrated that patients older than 75 years of age especially those with concomitant congestive heart failure have a higher risk of ablation-related complications.⁴⁹ With appropriate care in patient selection, age alone should not be considered a contraindication to recommending invasive options in patients with symptoms despite medical therapy.

Clinical Approach to AF Ablation in the Elderly

In our practice, just as with younger patients, when counseling the elderly for AF ablation, we stress the fact that this is potentially a quality of life improving technology and procedure. In other words, we emphasize that the procedure is not done to prevent stroke or prevent death but rather to help with symptomatic AF. If the elderly patient is symptomatic despite attempts at rate control and possibly a trial of one or more antirhythmic agents, we recommend radiofrequency ablation. Although this approach is similar to the one we use in younger patients, with the elderly, we typically give the option of AV node ablation and pacemaker insertion if rate control could not be achieved with pharmacological agents or rate control ameliorated symptoms of palpitation, however, the drugs could not be tolerated.

With regard to the invasive ablation approach, in the elderly, with paroxysmal AF, we typically perform pulmonary vein isolation and cavotricuspid isthmus ablation. Should there be other venous triggers of AF identified, these are mapped and ablated as well (superior vena cava, vein of Marshall). For persistent AF, left atrial linear lesions are also performed. Special care to avoid collateral damage especially to the esophagus is made with limiting ablation lesions in the posterior left atrium and ablating only as much as is required to diminish the local atrial electrograms. During the procedure, meticulous attention should be given to anticoagulation, and fluid management is essential in elderly patients, specifically over anticoagulation with increased risk of vascular access and pericardiac bleeding and avoidance of prerenal failure exasperating the often coexisting mild renal insufficiency in the elderly.⁷

Summary

Invasive management for symptomatic AF in the elderly is an important consideration to potentially improve quality of life. When the primary caregiver needs to counsel an elderly patient with AF on appropriate management strategies, the following steps should be undertaken:

1. Determine the appropriate choice for antico-

agulation.

2. An attempt at rate control to alleviate symptoms.
3. Consider rhythm control strategy with a pharmacological agent when patients remain symptomatic despite rate control.
4. Consider AV node ablation if rate control is not possible pharmacologically or is associated with intolerable side effects.
5. For those patients who remain symptomatic despite the above measures, AF ablation should be considered along with possible adjunctive pacemaker-based therapy.

Elderly patients should not be excluded from invasive therapy, as with appropriate caution these procedures can be performed with acceptable risk and a relatively high chance of alleviating symptoms. Patients, however, should be made aware that ablation is being offered purely for symptom-relief since there is no evidence to support invasive therapy purely to decrease mortality or to decrease stroke risk.

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