

Atrial Fibrillation: The Next Decade



Approximately 2.5 million patients in the United States and 3 million in Europe suffer from atrial fibrillation (AF). Due to the growing epidemic of obesity and other AF risk factors, this number is expected to grow to 16 million by the year 2050 in the US alone. Management of AF is very difficult to standardize; AF covers a wide spectrum of patients and is associated with a number of heart diseases. The contributing mechanisms have not been fully unraveled, and therefore one therapeutic modality is not universally appropriate. Understanding effective treatments of AF and how they can be improved

over the next several decades is critical to lowering this looming number.

Is there a future for antiarrhythmic drug therapy?

The majority of AF patients are over 65 years of age and are largely unable to endure surgical therapies. Therefore, argues Samuel Levy, MD, Chief of the Cardiology Division in the School of Medicine at Hôpital Nord, Marseille, France, “We DO need pharmacologic therapy.” Indeed, the AHA/ACC/ESC revised guidelines maintain that catheter ablation cannot be the first line of therapy. Finally, the ALFA study shows that in the “real world” (e.g. not in an academic institution where admitted patients are often difficult to treat), only about 30% of patients with paroxysmal AF are refractory to drug therapy.

Pharmacologic therapy is useful in controlling heart rate in patients in whom AF is well tolerated or chronic, and is as effective as rhythm control. The AFFIRM trial compared rate control and anticoagulation to medical therapies aimed at rhythm control and found that survival rates were similar. Therefore, controlling either rhythm or rate appears to be a valid goal.

One benefit of pharmacotherapy is that a patient can self-administer the drug outside of the hospital. This “pill-in-the-pocket” approach was tested (Alboni P et al; *NEJM* 2004; 351:2384) in a prospective study of recurrent AF where patients self-administered flecainide or propafenone. The results were very encouraging; 92% of episodes were treated effectively, there was a low rate of adverse events and a marked decrease in emergency room visits. This therapy is limited, however, to patients without ischemic heart disease or other significant structural heart disease.

*Highlights from the
American Heart
Association 2006
Scientific Sessions*

In France, 92% of patients with AF are taking some type of antiarrhythmic drug with amiodarone being the most widely used. Although it is very effective, many side effects are associated with amiodarone administration. Therefore, an iodine-free analogue, dronedarone, was developed and is currently in phase III clinical trials. This drug, estimates Dr. Levy, “has the highest chance to come to market.” The DAFNE (Dronedarone Atrial Fibrillation Study After Electrical Cardioversion) trial shows that a relatively high dose of 800mg effectively controls ventricular rate with very few side effects. Other drugs in development include Tedisamil, AZD7009 (Atrial Repolarization Delaying Agent; now in phase II testing) and CVT-510 (an A1 adenosine receptor agonist).

In summary, the first line of treatment for AF remains oral anti-coagulation and pharmacologic treatment for rhythm or rate control. Future therapeutic strategies, of which there may be many per patient, should be individually selected based on a safety first approach.

How will catheter ablation evolve over the next 10 years?

Ten years ago, AF was not related to mortality and was considered virtually harmless. “Now we know it is not a benign condition,” remarks Giuseppe Augello, MD, from the Department of Electrophysiology, San Raffaele Scientific Institute, Milan, Italy, “We need to treat AF in an evidence-based way and the first step is with antiarrhythmic drug (AAD) therapy. Catheter ablation is considered second line therapy for patients who are resistant to AAD therapy.”

There are many outstanding ablation techniques in use today, including pulmonary vein isolation (PVI) with a Lasso catheter, composite finite element (CFE) methods, and circumferential pulmonary vein ablation (CPVA). A recent study

of 77 patients receiving CPVA showed that 74% of patients were free of recurrent atrial fibrillation or flutter without AAD therapy (Oral H et al; *NEJM* 2006; 354:934). This study was limited to patients without significant structural heart disease such as low ejection fraction. In addition, while patients were followed with very careful arrhythmia monitoring the follow up was only 1 year. In the hands of the experienced operators, one third of patients required repeat ablation.

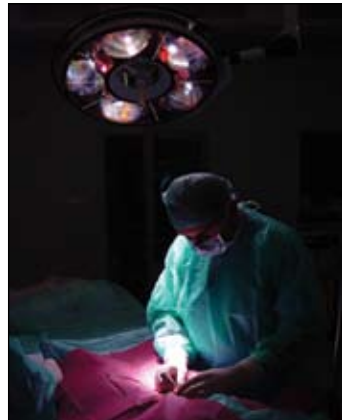
Surgical Approaches to AF

The Cox Maze III method, an open-heart surgical procedure to eliminate atrial fibrillation, has long been the gold standard for AF surgery. However, due to the amount of surgery required and the potential adverse outcomes, it is being phased out. A new procedure developed by Randall K. Wolf, MD, a cardiothoracic surgeon with the University of Cincinnati's Department of Surgery, termed the

In the next decade Dr. Augello estimates an insurgence of new technologies to treat AF, including:

- * Radio frequency ablation with irrigation
- * Selective ablation
- * Real-time MRI navigation
- * Robotic navigation
- * Automatic ablation
- * Network implementation
- * Individual pathophysiology
- * New ablation targets

minimize technique, is gaining attention. This minimally invasive procedure to cure AF obviates creating a large incision in the patient's chest and does not require a heart-lung machine.



“There have been two major changes in the treatment of AF”, says Dr. Wolf, “First, treat people with concomitant AF in the operating room (most common is a microvalve procedure) and second, offer some minimally invasive procedures for the stand-alone group.” The minimize technique, which involves opening the pericardium, takes about 2.5 hours and requires few or no incisions in the actual heart. In 2005, Dr. Wolf published encouraging results on this procedure performed on 27 patients (Wolf RK et al. *J Thorac Cardiovasc Surg* 2005; 130:797). A 91% cure rate was seen in the 23 patients that were available for a 6-month follow-up. Additionally, 90% of patients were cured for paroxysmal AF and 85% were cured for continuous AF at 3 years. Dr. Wolf estimates that over 1,700 cases have been performed worldwide and there have been no documented cases of mortality.

Careful planning and consideration can improve the outcomes of these procedures. Dr. Wolf emphasizes the importance of using intraoperative EP testing, adding, “It is important to have the equipment so that surgeons can speak the language of the electrophysiologist.” Removal of the left atrial appendage is also a very important part of Dr. Wolf’s procedure. Finally, careful selection of the energy sources and surgical techniques is vital. New techniques for atrial appendage exclusion, both percutaneous and surgical are also emerging (Gillinov AM et al. *Ann Thorac Surg* 2002; 74:2165

and Sievert H et al. *J Am Coll Cardiol* 2003; 41:(Suppl II):79A).

“I predict to you there will be a mushrooming of surgical data in 2007,” adds Dr. Wolf when commenting on the minimally invasive techniques for AF. The advantages of these techniques are that they address plausible mechanisms, are performed somewhat easily, have few complications and involve removal of the left atrial appendage.

How will we be treating AF in 10 years?

There are two approaches to treating AF, explains Gordon Tomaselli, MD, Professor of Medicine in the Department of Cardiology at Johns Hopkins University in Baltimore, Maryland. The primordial approach targets any underlying structural heart disease and the secondary approach is to prevent development and maturation of the disease. The following table delineates the strategies used today to treat AF and how they might evolve over the next 10 years.

	2006	2016
Cells and Genes	-Heritable AF which is just beginning to be understood -SNPs emerging -Experimental gene therapy only	-Better understanding of familial AF -Further cataloguing of predisposing SNPs -myocardial regeneration and repair
Drugs	-AADs -RAAS inhibitors -antioxidants -antihypertensives	-atrial specific AADs - evaluation of RAAS inhibitors -statins -PUFAs (fish oil) -novel agents
Catheters/ Scalpels	-SVT ablation -AF ablation -pacing	-improved imaging and catheter manipulation -hybrid ablation -randomized trial results to determine the role of catheter ablation in AF will be available