Atrial Fibrillation: Pathophysiology and Therapeutic Options

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INTRODUCTION TO ATRIAL FIBRILLATION – PREVALENCE, INCIDENCE AND RISK FACTORS

Atrial fibrillation was first described by William Harvey in 1628 as "auricular fibrillation" and was thought to be dissociation between the peripheral pulse and heartbeat. This later was recognized as an irregular pulse reflective of abnormal conduction, with the first case report published in the 1900s.[1] Since then, it has become one of the most studied arrhythmias. Today, atrial fibrillation is the most commonly encountered and clinically significant cardiac arrhythmia. Atrial fibrillation increases significantly with age, with nearly 1 in 25 people over the age of 60 and 1 in 10 over the age of 80 affected by this arrhythmia.[2] Studies show that the number of people with atrial fibrillation in the United States alone is estimated to be more than 2 million and projected to increase 3- to 5-fold, exceeding 10 million by 2050.[2–4] Furthermore, men are 1.5 times more likely to develop atrial fibrillation compared with women. In addition to age and sex, risk factors for developing atrial fibrillation include intrinsic cardiac disease, such as valvular pathology, left ventricular hypertrophy, myocardial infarction, and congestive heart failure; and noncardiac risk factors, such as smoking, hypertension, diabetes, and obesity.[2–5]

The focus of this article is to provide the practicing anesthesiologist with a detailed review of atrial fibrillation and therapeutic options. The topic is divided into 2 parts: the first focusing on the pathophysiology and the medical, interventional, and surgical interventions that currently are available, and the second focusing on the anesthetic management of patients for atrial fibrillation ablative therapy, including considerations for preoperative assessment, intraoperative management, and postoperative concerns.

DEFINITION—PAROXYSMAL, PERSISTENT, AND PERMANENT

One classification system, put forth by the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation[4] and the HRS/EHRA/ECAS 2007 Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation used to describe atrial fibrillation, involves the duration of the arrhythmia and its response to pharmacologic or electrical treatment. This system commonly is used in the context of catheter and surgical ablative therapy.[4,6] Paroxysmal atrial fibrillation is defined as episodic events that spontaneously terminate within 24 to 48 hours. Persistent atrial fibrillation is defined as lasting for >7 days, regardless of the use of pharmacologic treatment or cardioversion. A recent subset of this classification is a long-standing persistent atrial fibrillation in which the arrhythmia has been sustained for >1 year. Atrial fibrillation persisting for >1 year, in which cardioversion has failed or a decision has been made not to pursue restoration of sinus rhythm using electrical or ablative therapy, is termed "permanent atrial fibrillation" (Table 1).[4,6]

PATHOPHYSIOLOGY OF ATRIAL FIBRILLATION

The pathophysiology of atrial fibrillation is multifactorial, and a greater understanding of the mechanism has evolved over the past decade. Initially, the multiple-wavelet hypothesis was thought to induce atrial fibrillation. This theory is based on the generation of multiple wavelets of electrical activity in the right and left atria that are able to initiate and sustain irregular atrial activity. A critical mass, and, therefore, critical number of wavelets is required to sustain the arrhythmia.[1,4,6,7] However, an alternative theory states that a small number of high-energy reentrant circuits, usually found in the left atrium, also can generate some cases of atrial fibrillation. The rapid activation of these circuits can overcome regular atrial activity and lead to the disorganized rhythm.[8,9]

A newer theory, providing the theoretical basis for understanding the mechanism of how catheter ablation therapy works, is centered on the idea of a single electrical focus or a few foci. The rapidly discharging foci are thought to initiate irregular electrical activity through the atria, leading to fibrillatory conduction. Although the most common origin of this focal activity is the pulmonary veins, other areas, such as the wall of the right and left atria, interatrial septum, the coronary sinus, and superior vena cava also have been implicated.[6,7,9]

The pulmonary veins play a central role in atrial fibrillation through the mechanism of automaticity and triggering potential. The cardiomyocytes in the pulmonary veins have been shown to develop pacemaker-like activity, resulting in spontaneous depolarization and/or microreentry circuits. Furthermore, the different electrophysiologic construction in susceptible myocardium

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Table 1. Definitions of Atrial Fibrillation

Acute	Onset within the previous 48 hours.
Paroxysmal	Spontaneous termination within 7 days and most often within 48 hours. Paroxysmal AF may degenerate into a sustained form of AF.
Recurrent	Two or more episodes, which may be defined as paroxysmal if they terminate spontaneously or persistent if the arrhythmia requires electrical or pharmacologic cardioversion for termination.
Persistent	Not self-terminating; lasting longer than 7 days, or prior cardioversion. Persistent AF may degenerate into permanent AF.
Permanent	Long-standing AF (defined as more than a year) that is not terminated successfully by cardioversion, when cardioversion is not pursued, or has relapsed following termination.

NOTE. Categories as defined by the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation executive summary and HRS/EHRA/ECAS 2007 Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation.

Abbreviation: AF, atrial fibrillation.

affects the refractory period and conduction velocity through the atrium, resulting in irregular electrical activity.[4,10–12]

An important factor in the pathogenesis of irregular conduction leading to atrial fibrillation is increased parasympathetic activity. Although sympathetic adrenergic tone regulates the maintenance of fibrillatory activity, recent evidence suggests that initiation of atrial fibrillation is attributed to cholinergic stimulation.[13] Parasympathetic activity is mediated by autonomic fibers that innervate the atria and can be stimulated by an increase in vagal tone. These nerve fibers also can be affected by many pathologic states, such as congestive heart failure and mitral valve disease, leading to increased left atrial pressures resulting in atrial stretch. These factors can facilitate focal pulmonary vein electrical activity and affect the atrial refractory period and the conduction velocity abnormalities associated with atrial fibrillation.[4,6,8,9,13]

Sustained atrial fibrillation can lead to abnormalities in the effective refractory period and in the underlying atrial electrophysiologic substrate. This process is known as electrophysiologic atrial remodeling, resulting in atrial dilatation and fibrosis. Ultimately, advancement of atrial remodeling results in progressive shortening of the refractory period and increased duration of irregular activity, leading to persistent atrial fibrillation.[4,9]

MORBIDITY AND MORTALITY OF ATRIAL FIBRILLATION

Atrial fibrillation is a significant source of morbidity and mortality in the elderly. This common arrhythmia is associated with an increased incidence of cardiomyopathies, leading to heart failure and reduced overall quality of life secondary to symptoms such as palpitations, shortness of breath, chest pain, and fatigue. Hemodynamic abnormalities, including reduced cardiac output, atrioventricular valvular regurgitation, reduced atrial contribution to ventricular filling, and increased left atrial pressures, further add to the morbidity of atrial fibrillation. Many of these adverse hemodynamic effects, secondary to factors such as loss of atrioventricular (AV) synchrony, irregular ventricular rhythm, and irregular R-R intervals, are independent of heart rate.[6,14] Atrial fibrillation also has been shown to be an independent contributor to dementia and cognitive dysfunction[3,15] and strongly linked to premature death. Patients with atrial fibrillation have a markedly reduced survival rate, with a 1.5- to 1.9-fold mortality risk even after adjustment for cardiovascular risks such as age, sex, hypertension, smoking, diabetes, left ventricular hypertrophy, myocardial infarction, congestive heart failure, valvular heart disease, and stroke.[16]

A significant source of morbidity strongly associated with atrial fibrillation is stroke. Chronic atrial fibrillation has been shown to greatly increase risk of cerebral embolism, accounting for up to 50% of cardioembolic strokes.[17–20] Furthermore, 1 in every 9 patients thought to have a cryptogenic ischemic stroke was detected to have underlying paroxysmal atrial fibrillation during long-term electrocardiogram (EKG) monitoring.[21] Studies show that 35% of patients with nonvalvular or nonrheumatic atrial fibrillation will experience an ischemic stroke during their lifetime. Compared with patients in sinus rhythm, patients with atrial fibrillation with no rheumatic heart disease have more than a 5-fold increase in stroke risk, while patients with rheumatic heart disease and atrial fibrillation have more than a 17-fold increase in stroke incidence.[17,20,22,23] In addition, atrial fibrillation is an independent risk factor for stroke, especially with age, showing an increase from 1.5% for those aged 50 to 59 years to 23.5% for those aged 80 to 89 years.[24,25]

MEDICAL TREATMENT

Pharmacologic therapy has been the mainstay of treatment for atrial fibrillation. Therapy consists of 3 main strategies: rhythm control, rate control, and anticoagulation. Often, more than 1 approach is necessary for the treatment regimen. The theoretical advantages of restoring sinus rhythm include symptom relief, improvement of patient hemodynamics, and possible decrease in risk of embolic events. Rhythm control involves either electrical or pharmacologic cardioversion and treatment with antiarrhythmic drugs to maintain sinus rhythm. Numerous antiarrhythmic agents have been used for the maintenance of sinus rhythm. Unfortunately, the lack of efficacy and side effects of many antiarrhythmic drugs make them a less attractive option for the treatment of atrial fibrillation. One of the later agents, amiodarone, has gained in popularity due to its efficacy and better side effect profile. Many studies have shown amiodarone to be superior in maintaining sinus rhythm and even useful in rate control with fewer side effects compared with older agents, such as flecainamide, sotalol, and propafenone.[26–28] However, the lipophilicity and iodine moieties in amiodarone make it potentially toxic to the thyroid, lungs, liver, cornea, and peripheral nervous system.[29–31]

Dronedarone is a noniodinated congener of amiodarone without many of the side effects associated with amiodarone use. Dronedarone is a class III antiarrhythmic agent and a