Different Electrophysiological Alterations of the Atrial Myocardium Depending on the Underlying Baseline Disease in Patients with Paroxysmal Atrial Fibrillation

Introduction

Atrial fibrillation (AF) is a common arrhythmia, and its incidence rises sharply in the elderly population. Degenerative changes of the atrial myocardium observed in pathological studies were reported to be associated with an increased incidence of AF with advancing age [1-3]. It is often impossible to separate physiological aging alterations from the development of pathological changes due to a comorbid disease. For example, lone paroxysmal atrial fibrillation has no identifiable underlying cause, and can occur any time for no apparent reason. However, paroxysmal atrial fibrillation (PAF), being the most common arrhythmia in the clinical setting, is usually a consequence of established heart disease. It is frequently associated with different cardiac diseases, namely, ischemic heart disease, cardiomyopathy, pericardial disease, valvular heart disease, hypertension, congestive heart failure, preexcitation syndrome, and sinus node dysfunction [4-8].

The PAF incidence clearly increases three-to-fivefold when cardiovascular disease occurs. PAF was most commonly a consequence of rheumatic heart disease with mitral stenosis in the past. Moreover, non-cardiac conditions, namely, aging, autonomic tones, cholinergic drug use, thyroid function, acute alcohol intoxication, metabolic or electrolyte disturbances, surgery or diagnostic procedures, and drugs, also affect initiation, maintenance, and termination of AF. Although these underlying causes may modify the electrophysiological properties of the atrium, there has been little information on the relationship between the atrial electrophysiological properties and predisposing conditions for AF. Interesting investigations on atrial fibrillation development have been done in the context of open heart surgery. Although a reentrant activation sequence of multiple wavelets has been demonstrated in human AF by epicardial mapping just before the surgical treatment of this arrhythmia [5, 6], the method is not suitable or feasible for diagnostic or investigational purposes in the clinical electrophysiologic laboratory. Therefore, clinical electrophysiologic studies have focused mainly on the electrophysiologic properties of the substrates in the atrial muscle during sinus rhythm and on the atrial electrical responses elicited by the premature stimulation method. A wealth of new information has been published on the genesis of AF, such as repetitive atrial firing, fragmented atrial activity, and intraatrial conduction delay, and have been observed more frequently in patients with paroxysmal AF than in those without [16-18]. Shorter atrial effective refractory periods have been also shown to be of electrophysiological significance in the genesis of AF.

It has been shown that the initiation, maintenance, and termination of AF were affected by many modifying factors of the electrophysiologic properties at the atrium. The increase in prevalence of PAF in elderly persons has been reported to be associated with degeneration of the atrial muscle in pathologic studies [19]. Spach and Dolber [20] found evidence in the human atrial muscle of an age-related electrical uncoupling of the side-to-side connections between bundles, related to the proliferation of extensive collagenous tissue septa in intercellular spaces. Abnormal atrial electrograms recorded by endocardial mapping during sinus rhythm, abnormal responses of the atrium elicited by programmed stimulation, shorter atrial effective refractory periods, greater dispersion of atrial refrac-
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Toriness and atrial conduction delay have been observed more frequently in patients with paroxysmal AF [21-27]. However, even if atrial electrical remodeling facilitates AF initiation and maintenance, the initiation of AF requires a trigger. Perhaps, the greatest advancement in our understanding of atrial fibrillation relates to the demonstration that ectopic foci from the pulmonary veins are the main triggers of AF [7-10].

AF assumes a great clinical importance in the setting of Wolff-Parkinson-White (WPW) syndrome because of the potential risk for ventricular fibrillation, circulatory collapse, and sudden death [25]. It has been suggested that the accessory atrioventricular pathways may participate directly in the induction of AF [28]. On the other hand, Fujimura et al. [29] reported longer intra-atrial conduction times and shorter atrial functional refractory periods in the patients with WPW syndrome associated with paroxysmal AF than in those without paroxysmal AF. Koene et al. [30] demonstrated a significantly longer duration and greater number of fragmented deflections of atrial endocardial electrograms in patients with AF associated with WPW syndrome than in those with WPW syndrome alone. These findings suggest that the intrinsic electrical abnormalities of the atrial muscle may play an important role in the occurrence of paroxysmal AF in patients with WPW syndrome.

All the other cardiac conditions, namely, hypertension, valve disease, thyrotoxicosis, and congestive heart failure are also important modifying factors for the electrophysiologic properties of the atrial muscle. However, there has been little information on the relationship between the electrophysiologic substrate and underlying cardiac diseases. AF was induced in 11% of patients with hypertrophic cardiomyopathy during electrophysiological study [31]. Patients with hypertrophic cardiomyopathy are prone to develop AF due to worsening diastolic dysfunction and left atrial dilatation rather than as a primary electrical phenomenon [32]. Li et al. [33] reported a unique study to test the hypothesis that AF maintained by different substrates responds differently to antiarrhythmic-drug therapy. These results indicate that electrophysiologic properties of AF are different for the different types of underlying disease in AF. These findings have direct clinical implications regarding adequate management of antiarrhythmic drugs, giving insight into correct choosing of antiarrhythmic agent.

In conclusion, PAF is caused by various underlying disorders. Several studies indicate that electrophysiologic properties of AF are different for the different types of underlying disease in AF. Patients with PAF exhibit an electrophysiologic diversity of the atrium in conjunction with their complication status, and insight into these electrophysiologic abnormalities will help in determining effective antiarrhythmic drugs for these patients. Further investigation into the electrophysiologic properties in AF will be needed in order to contribute to the future development of an appropriate medical and interventional treatment.

References