

Atrial Electrophysiological Modifications Generated by a Single Atrial Premature Contraction

Abbreviations: APC: Atrial Premature Contractions; AF: Atrial Fibrillation; RAF: Repetitive Atrial Firing; FAA: Fragmented Atrial Activity; ACD: Inter-Atrial Conduction Delay

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Most of the patients who undergo a Holter ECG ambulatory monitoring study are found to have atrial premature contractions (APC). Although it is not worrisome if the patient has no organic heart disease, it is wise to think that a simple APC can produce changes in atrial electrical conduction that may alter the depolarization pathway in different manners eliciting reentry. The use of programmed atrial stimulation with single atrial extra-stimulus was undertaken as a way of understanding the electrophysiological properties of the atrium [1-3]. Although this is a procedure that we have been doing for decades, it is always healthy to return to the basics and meditate from the beginning. Furthermore, it is a procedure that has passed the test of time. This mimics in the laboratory what is produced clinically when an APC occurs in the patient.

Since the modifications produced by an APC may be significant in certain patients with altered atrial muscle vulnerability, it is important to concentrate on the electrical changes that a simple APC can induce. With programmed atrial stimulation, we are able to record atrial activation times, atrial conduction intervals, different types of delays in atrial conduction, dispersion of atrial refractoriness, and different kinds of atrial responses that alter atrial electrical conduction paving the way to reentry mechanism for arrhythmia. After a premature atrial beat delivered at a critical coupling interval, several responses, such as repetitive atrial firing, fragmented atrial activity, atrial conduction delay, and atrial fibrillation (AF) can be elicited. Patients with paroxysmal AF not only have been found to have a higher incidence, but also to have significantly wider zones, of these parameters than the control subjects. Therefore, the widening of these zones may be closely related to the spontaneously occurring episodes of AF [1-5]. The abolition or reduction of the zone of these markers of atrial vulnerability by antiarrhythmic agents may indicate the usefulness of a drug in preventing the initiation of AF.

Repetitive atrial firing (RAF) often precedes atrial flutter or degenerates to AF [4-9]. Several clinical studies have demonstrated that RAF is a common finding in patients with paroxysmal AF [4-6]. According to Wyndham et al. [7], RAF is defined as the occurrence of two or more successive atrial complexes with a return cycle of <250 ms and a subsequent cycle length of <300 ms. The mechanism of RAF appears to be a local reentry around the point of stimulation in a double circuit "figure-of-eight" pattern, as has been shown in experimental studies that have used a rabbit atrium and an open-chest dog [10]. Other mechanisms, such as triggered activity or enhanced automaticity, also have been described as

Mini Review

Volume 3 Issue 4 - 2015

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Received: October 05, 2015 | **Published:** October 12, 2015

possible mechanisms [11]. Atrial premature stimulation seemed to facilitate the induction of RAF both by promoting intra-atrial conduction delays, as well as by shortening the atrial refractory period [5]. Shimizu et al. [8] observed that the effective refractory period was significantly shorter at sites where RAF was induced than at sites where it was not induced. RAF reportedly occurred in 94% of the atrial sites with an effective refractory period of <260 m sec and a maximum conduction delay >40 msec. These results suggest that the occurrence of RAF requires the presence of a short refractory period at the pacing site and prolongation of the maximum conduction delay [8,12].

A single atrial extra stimulus often results in widening of the local atrial electrogram, namely, fragmented atrial activity (FAA). It has been demonstrated that fragmentation and slowing of conduction in response to premature stimulation are related to paroxysmal AF [1,2,13]. Fractionated auricular electrograms are recorded from myocardial sites where auricular muscle fibers are widely separated by fibrosis that has resulted from ischemia, inflammation, or degeneration [14]. Ohe et al. [1] defined FAA elicited by atrial extra stimuli as the occurrence of disorganized atrial activity >150% of the duration of the local atrial electrogram of the basic beat recorded in the right atrium. The duration of the local atrial electrogram and the induction zone of FAA are greater in patients with PAF than in controls [1,2]. Although FAA also is elicited in subjects without paroxysmal AF, the widening of FAA zone is characteristic of paroxysmal AF. FAA may be a good indicator of a tendency to develop spontaneous AF [1]. Electrophysiological studies performed in patients with chronic sustained lone AF after electric cardio version also has shown a wider FAA zone than that in controls [3].

The slowing of intra-atrial conduction is considered to be one of the most important requirements for the initiation of reentry and, thus, for AF or atrial flutter to develop [2,8]. Inter-atrial conduction delay (ACD), measured from the stimulus artifact to

the atrial electrogram at the coronary sinus distal level, reflects an actual ACD that is not influenced by local latency at the site of stimulation [8]. Hashiba et al. [13], by using a rigid criterion for ACD (the S₂ through A₂ increments >50 m sec), found a significantly greater incidence of ACD in patients with paroxysmal AF than in controls. It is important to note that a significantly wider zone of ACD was observed in patients with paroxysmal AF than in controls [2,12].

Bi-atrial pacing was developed as a technique of simultaneous activation of the right atrium and left atrium to reduce the ACD [15-19]. This procedure has been reported to prevent the recurrence of AF in paced patients with marked ACD [16]. Therefore, these facts indicate that the ACD can play an important role in the onset of AF. On the other hand, controversy has existed for a long time regarding whether AF was due to a single focus firing rapidly or to some sort of reentrant excitation. This arrhythmia might result from some combination of the two. It is now generally accepted that ectopic foci from the pulmonary veins can initiate AF and can also act as drivers for maintaining AF [20-24]. However, not all patients with atrial arrhythmias initiate AF. A substrate for atrial propensity to AF is required for AF initiation and maintenance. AF results from a critical number of simultaneously circulating wavelets, the so-called multiple-wavelet hypothesis proposed by Moe et al. [25]. Several investigators were able to record atrial activation times, atrial conduction intervals, different types of delays in atrial conduction, and dispersion of atrial refractoriness. Allesie et al. [26] have provided clear evidence to support the multiple-wavelet hypothesis as the basis of AF by multisite mapping studies with a Langendorff-perfused canine atrial preparation of AF induced by rapid pacing and sustained by acetylcholine infusion [26]. They emphasized the importance of a critical number of simultaneously circulating wavelets of the random reentry type and the importance of activation of each atrium by wavelets from the other atrium. On the basis of the pattern of activation obtained by simultaneous multisite mapping during induced AF in human AF, Konings et al. [27] distinguished three types of AF based on activation patterns. In type I, the right atrial free wall was activated by single broad wave fronts propagating without conduction delay. Type II was more complex, showing a higher degree of delayed conduction and intra-atrial conduction block. Type III activation was highly complex, with three or more wavelets associated with areas of slow conduction and conduction block. Moreover, it was suggested that AF might be generated by one or possibly two unstable reentrant circuits of short cycle length [28-31]. There is an interaction in which unstable and short-lived reentrant circuits (mother waves) of short cycle length generate wave fronts (daughter waves), which serve to re-form the unstable reentrant circuits. It is because the unstable reentrant circuits are always generating multiple wave fronts and the wave fronts are continuously re-forming reentrant circuits of short cycle length that AF is maintained in this type of model [29-32].

A better understanding of the mechanism of initiation and maintenance of AF mediated by an APC may provide insights into devising therapeutic strategies for the treatment of AF. Their mapping data may provide new insights into the decision of where anatomically to place the critical incisions or even

ablative lesions in patients with paroxysmal AF. Several abnormal responses have been elicited by premature atrial stimulation, including RAF, FAA, and ACD and can develop under a clinical APC. Although these responses do not show the localization and characteristics of reentry circuits, they are found to be closely related to the development and maintenance of AF in predisposed patients. These indicators of atrial vulnerability and their corresponding zones of induction are useful parameters indicative of predisposition to AF. Electrophysiological studies in patients with paroxysmal AF have led to essential understanding of the underlying clinical physio-pathologic process of AF [33-37]. The abnormal responses elicited by a single APC have been observed more frequently in patients prone to develop paroxysmal AF. The specificity, sensitivity, positive and negative predictive values of these abnormal responses for episodes of AF remains controversial. However, their corresponding zones have been considered to be useful parameters as substrates of development of AF. Therefore, it is wise to clearly understand that a simple APC can produce changes in atrial electrical conduction that may alter the depolarization pathway in different manners eliciting reentry. Those changes may be profound in certain patients with altered atrial muscle vulnerability.

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