Mechanisms for the genesis of paroxysmal atrial fibrillation in the Wolff–Parkinson–White syndrome: intrinsic atrial muscle vulnerability vs. electrophysiological properties of the accessory pathway

Osmar Antonio Centurión1*, Akihiko Shimizu2, Shojiro Isomoto3, and Atsushi Konoe4

1Division of Electrophysiology and Arrhythmias, Cardiovascular Institute, Sanatorio Migone-Battilana, Asuncion, Paraguay; 2Faculty of Health Science, Yamaguchi University School of Medicine, Ube, Yamaguchi, Japan; 3Department of Cardiovascular Science, Oita University School of Medicine, Oita, Japan; and 4Third Department of Internal Medicine, Nagasaki University School of Medicine, Nagasaki, Japan

Received 20 November 2007; accepted after revision 19 January 2008

Background Paroxysmal atrial fibrillation (PAF) develops in up to one-third of patients with the Wolff–Parkinson–White syndrome (WPW). The reason for this high incidence of PAF in the WPW syndrome is not yet clearly understood. When PAF appears in patients with WPW syndrome who have anterograde conduction via the accessory pathway (AP), it may be life-threatening if an extremely rapid ventricular response develops degenerating into ventricular fibrillation.

Methods and results Several mechanisms responsible for the genesis of PAF in WPW patients were hypothesized, namely, spontaneous degeneration of atrioventricular reciprocating tachycardia into atrial fibrillation (AF), electrical properties of the APs, effects of APs on atrial architecture, and intrinsic atrial muscle vulnerability. Focal activity, multiple reentrant wavelets, and macroreentry have all been implicated in AF, perhaps under the further influence of the autonomic nervous system. AF can also be initiated by ectopic beats originating from the pulmonary veins, and elsewhere. Several studies demonstrated a decrease incidence of PAF after successful elimination of the AP, suggesting that the AP itself may play an important role in the initiation of PAF. However, PAF still occurs in some patients with the WPW syndrome even after successful elimination of the AP. There is an important evidence of an underlying atrial disease in patients with the WPW syndrome.

Conclusions Atrial vulnerability has been studied performing an atrial endocardial catheter mapping and analysing abnormal atrial electrograms. Other studies evaluated atrial refractoriness and intraatrial conduction times, suggesting an intrinsic atrial vulnerability as the mechanism of PAF and considering the AP as an innocent bystander. It is our intention to analyse the available data on this particular and interesting topic since AF has a singular prognostic significance in patients with the WPW syndrome, and its incidence is unusually high in the absence of any clinical evidence of cardiac organic disease.

KEYWORDS Paroxysmal atrial fibrillation; Wolff–Parkinson–White syndrome; Atrial vulnerability; Accessory pathway; Abnormal atrial electrograms

Introduction

Séneca, a renowned roman philosopher, wrote the following words in the first century: ‘Death is sometimes a punishment, frequently a gift, and for many a favor’. Evidently, unexpected death of a young healthy person without organic heart disease can never be a gift, nor be a favor ever. It is an incomprehensible and inconceivable disgrace for the family and the society. The painful feeling deepens, and the frustration and impotence exacerbate when it turns out to be a death that could have been prevented.

Paroxysmal atrial fibrillation (PAF) develops in up to one-third of patients with the Wolff–Parkinson–White (WPW) syndrome.1,2 The reason for this high incidence of PAF in the WPW syndrome is not yet clearly understood. When PAF appears in patients with WPW syndrome who have anterograde conduction via the accessory pathway (AP), it may be life-threatening if an extremely rapid ventricular response develops degenerating into ventricular fibrillation.3 Several mechanisms responsible for the genesis of
PAF in WPW patients were hypothesized, namely, spontaneous degeneration of atrioventricular reciprocating tachycardia (AVRT) into atrial fibrillation (AF), electrical properties of the AP, effects of AP on atrial architecture, and intrinsic atrial muscle vulnerability.¹⁻⁹

Spontaneous degeneration of AVRT into AF has been observed during electrophysiological studies in a minority of patients with WPW syndrome. On the other hand, PAF is often observed in patients without AVRT. Several studies demonstrated a decrease incidence of PAF after successful elimination of the AP, suggesting that the AP itself may play an important role in the initiation of PAF. Therefore, the existence of a functional AP and inducible AVRT has been found to play an important role in triggering AF in the WPW syndrome. However, PAF still occurs in some patients with the WPW syndrome even after successful definitive elimination of the AP. This fact questions whether the elimination of AP is the true mechanism by which the incidence of PAF is reduced in WPW patients.

There is an important evidence of an underlying atrial disease in patients with the WPW syndrome. Some investigators have studied the atrial vulnerability performing an atrial endocardial catheter mapping and analysing the recorded abnormal atrial electrograms.¹⁰⁻¹² Others have investigated the atrial electrophysiological substrate that may predispose to PAF appearance. Atrial refractoriness and intraatrial conduction times were evaluated, suggesting an intrinsic atrial vulnerability as the mechanism of PAF and considering the AP as an innocent bystander. Age seems to be the most clinically relevant predictor of continued AF after ablation of the pathway, and this is probably in part because AF is the presenting arrhythmia and the pathway a relatively innocent bystander. Konoe et al.⁴ found that the mean age of the patients with WPW syndrome and PAF was significantly higher than that of WPW patients without PAF.

It is our intention to analyse the available data on this particular and interesting topic since AF has a particular prognostic significance in patients with the WPW syndrome, and its incidence is unusually high in the absence of any clinical evidence of atrial disease. Therefore, we will examine the available evidence and analyse the role of the AP, as well as, the role of atrial vulnerability in the genesis of PAF in patients with the WPW syndrome.

**Role of the accessory pathway and its branching network**

There is considerable evidence that point to the electrophysiological properties of the AP as an important factor in the genesis of PAF in the WPW syndrome. Excitation inputs into the atrium over a retrograde multiple or multifibre AP during AVRT could precipitate initiation of PAF.³,¹³ The coexistence of a functional AP and sustained episodes of AVRT has been found to play an important role in triggering AF in patients with the WPW syndrome. The incidence of spontaneous degeneration of induced AVRT into AF has been reported to be in the range of 16–26% occurring in a similar proportion in patients with concealed WPW, and manifests WPW syndrome.³,¹⁴ It has been shown that AVRT can increase atrial vulnerability as a result of a shortened atrial cycle length, increased sympathetic tone and atrial stretch because of haemodynamic changes that occur during AVRT. Chen et al.¹⁵ observed that the AVRT cycle length at the time of electrophysiological study was significantly shorter in WPW patients with than without AF. This finding suggests that it is easier to develop PAF in a rapid episode of sustained AVRT. Long-term follow-up studies after successful surgical or catheter ablation of the AP have shown significantly reduced incidences of spontaneous PAF. The recurrence rate of spontaneous PAF after successful ablation of the AP is reported to be in the range of 6–10%.¹⁻³ In this respect, Hamada et al. observed that clinical episodes of PAF recurred in 71% of their patients whose AF remained inducible post-ablation, however, in none of the patients who remained uninducible post-ablation.¹⁶ Therefore, there is a high incidence of AF recurrence in a subgroup of patients whose AF remains inducible despite successful ablation of the AP. A detailed examination of this subgroup of patients prone to develop AF could shed more light in the understanding of the mechanisms for the genesis of PAF in WPW patients despite successful AP ablation.

**Retrograde electrophysiological properties of the accessory pathway**

The retrograde electrophysiological properties of the AP have been well investigated. Campbell et al. described in detail the role of retrograde multiple AP as a mechanism of premature atrial contraction that initiates atrial repetitive firing or intra-atrial reentry in the vulnerable period of the atrium during AVRT.¹³ They speculated that intermittent retrograde conduction over a second AP with faster conduction caused early atrial depolarization. They also demonstrated a high incidence rate of AF that was initiated with incremental right ventricular pacing and premature ventricular contraction (PVC). Hsieh et al.⁷ investigated the influence of atrial double potentials in the genesis of AF in patients with WPW syndrome. Double atrial potentials recorded in the coronary sinus are not an unusual phenomenon in patients with supraventricular tachyarrhythmias and have been demonstrated to potentiate the occurrence of arrhythmias. They demonstrated that patients with the WPW syndrome, especially with a left lateral bypass tract, had a higher incidence of double atrial potentials, and induced AF than patients with AVNRT. Furthermore, WPW patients with double atrial potential had a higher incidence of induced AF than those WPW patients without it. Spontaneous occurrence of PVC depolarizes the atrium in a retrograde manner that can cause AF to develop. Jackman et al. indicated that microreentry mimicking atrial flutter or fibrillation could originate within the branching networks of the AP strands and that this may account for the unusually high incidence of AF in the WPW syndrome.¹⁷ They utilized closely spaced orthogonal catheter electrodes in the coronary sinus and found electrophysiological evidence for a branching or multifibre structure of the left free wall AP. They also observed multiple retrograde conductions over separate AP branches during AVRT and reentry originating from the branching networks. However, this finding has not been confirmed in a large population. Moreover, this finding was indirectly contradicted by Wathen et al.¹⁸ and Ong et al.¹⁹ since they showed in mapping studies of AF initiation in patients with the WPW syndrome that the onset of AF was more frequently initiated near the high right atrium regardless of the AP location. Fujimura et al.³ also demonstrated that most episodes of AF started at a high
right atrial site regardless of AP location, with only 19% of AF episodes starting at the electrode site in the coronary sinus closest to the AP. Iesaka et al. found that the incidence of clinical PAF as well as induced AF was significantly greater in patients with multiple AP. However, the incidence of clinical AVRT was similar between multiple and single AP patients. The incidence of AF initiated during ventricular pacing and AVRT was significantly greater in the multiple AP patients. A very interesting finding in this study was that AF inducibility during AVRT and ventricular pacing was eliminated by partial ablation of multiple or multifibre AP. However, AVRT inducibility remained in most patients with partial ablation of the multiple or multifibre AP. The incidence of induced AF after total ablation was similar between patients with multiple or single AP. Ong et al. performed an atrial mapping study using a multiple electrode array during surgery and suggested a possible mechanism of sustaining AF in patients with WPW syndrome. They demonstrated that wavefront collisions between incoming atrial wavefronts via an AP during non-pre-excited beats generated new wavefronts to help perpetuate AF. This concept of intra-atrial wavefront collision possibly explains susceptibility to AF in patients with multiple AP. Multiple and asynchronous wavefronts could be generated by retrograde conduction over multiple AP or widely separated strands forming multifibre AP during AVRT. The wavefront collision in the atrium could be a mechanism for induction and perpetuation of AF. Although, it seems a plausible conception the exact electrophysiological mechanism remains to be clarified in detail.

Anterograde electrophysiological properties of the accessory pathway

Other studies reported findings that stressed the relation between anterograde conduction properties of the AP and AF. Fujimura et al. observed that the anterograde AP effective refractory period (ERP) was shorter in the group with AF than in the control group, and that there were no significant differences in retrograde properties. Other investigators also reported similar findings. They also found that AF was more frequent in patients with manifest WPW than in those with concealed WPW syndrome. These findings suggest that the retrograde conduction properties of a single AP are not the critical determinants of AF. The anterograde AP conduction properties distinguished patients with and without AF. It is known that a shorter anterograde AP ERP allows faster ventricular rates during AF, therefore, the associated atrial stretch and hypoxia may contribute to sustaining the arrhythmia.

The effects of accessory pathway on atrial architecture

It is well known that structural heterogeneities play an important role in atrial reentry because of the influence of unidirectional block and conduction delay. Thus, it is possible that in patients with WPW syndrome, the increased structural heterogeneity created by the presence of the AP may play a role in the generation and maintenance of atrial reentry. In experimental studies of the canine heart model of WPW syndrome, structural differences in the AP apparently affected refractoriness and conduction properties of the pathway. Until now, no detailed data on the structure of atrial tissue around the AP have been available. Most of the histopathological studies in patients with WPW syndrome have dealt with the AP itself. It was postulated that the AP is the result of an embryological fault in the formation of fibrous tissue separating the atria and the ventricles. Therefore, developmental abnormalities may also be present in the atrial tissue adjacent to the AP, which may affect the functional electrical properties of the atrium close to the AP. Dispersion of the refractory periods and conduction disturbances apparently occur around the interconnection between different tissues such as the atrium and the AP. Either anatomical or functional properties of the atrial tissue near the AP may play a role in the genesis of AF and may contribute to the different incidence of atrial vulnerability and AF in the WPW syndrome. This is a field that needs further investigation.

Different anatomical sites of the accessory pathway

The location of the AP was also related to the induction of AF. It was shown that patients with an anteroseptal AP had a high rate of inducible arrhythmia (62%). Patients with a right free wall AP had a rather low rate of inducible arrhythmia (21%). Patients with left free wall and posteroseptal AP had a 44 and 36% rate of induction, respectively. Patients with a right-sided AP had a lower inducibility of AVRT and a relatively long retrograde ERP over the AP. This allowed only relatively late PVCs to be conducted retrogradely over the AP to the atria, which might explain the lower rate of inducibility of AF in these patients.

Role of the intrinsic atrial muscle vulnerability

Atrial fibrillation has a particular prognostic significance in patients with the WPW syndrome, and its incidence is unusually high in the absence of any clinical evidence of atrial disease. It has been shown that recurrences of AF after successful AP ablation occur at a low incidence. Although, for most WPW patients the AP ablation is a curative solution, sustained episodes of AF still occur in certain patients despite the disappearance of the AP. Therefore, it is very important to determine all possible mechanisms for the development of PAF in the WPW syndrome patients. An explanation suggested, in certain patients, is the presence of an underlying atrial disease considering the AP as an innocent bystander. In the absence of structural atrial disease, clinical electrophysiological studies have not clearly defined atrial features that can predict spontaneous occurrence of AF. Some investigators have studied the atrial vulnerability showing that the induction of sustained episodes of AF was more frequent in patients with a history of spontaneous AF. Others have analysed the atrial electrophysiological substrate that may predispose to AF. They evaluated atrial refactoriness, intra- and inter-atrial conduction times, and several electrophysiological parameters elicited with programmed atrial stimulation with single extrastimulus. It was demonstrated that WPW patients with PAF have intrinsic atrial muscle abnormalities and most of them present abnormally prolonged and fractionated atrial electrograms that are recorded with atrial endocardial mapping (Figure 1).

With a computer model of AF, Moe et al. showed that an atrial condition characterized by short and non-homogeneous atrial ERP, associated to intra-atrial.
activity and reentry became higher. These various types of AF in humans appear to be characterized by different numbers and dimensions of the intra-atrial reentrant circuits. Clinical electrophysiology has identified several atrial features that may lead to the appearance and maintenance of AF, sometimes with conflicting results. These different results may be because of multiple factors, including different stimulation protocols and non-homogeneous groups of patients.

Atrial refractoriness in atrial fibrillation

Several studies have shown conflicting results regarding refractoriness in AF. The measurement of atrial ERP in AF patients in only one site does not necessarily represent atrial refractoriness since these patients have a wide dispersion of atrial refractoriness. Therefore, it is not comparable in different sites of the atrium neither in different patients. Some investigators reported short atrial ERP in patients with PAF, whereas others did not. Thus, it is controversial to utilize atrial ERP as a useful measure of atrial vulnerability. Some reports have shown that the atrial ERP physiologically shortens with increasing heart rate. This rate adaptation is less evident in AF patients, as well as, in isolated cellular preparations. Riccardi et al. evaluated the rate adaptation of ERP in WPW patients with and without AF, analysing the gradient between two different atrial pacing cycle lengths. They found that the functional refractory period increased in most AF patients (81%) with an increase of the atrial stimulation rate, although this absent rate adaptation was observed only in few patients (24%) without AF. The fact that WPW patients with AF showed higher values of refractory periods, which became even higher with increasing heart rate, suggests the concept of AF as based on slow conduction through partially recovered myocardium. Muraoka et al. observed that the atrial ERP was prolonged, the zones of atrial vulnerability were narrowed, and the induction rate of AF was reduced following the elimination of the AP by surgical cryoablation. However, these parameters were unchanged in patients that had their AP ablated by radiofrequency catheter ablation. Although they could not clearly explain these different findings with the different ablation techniques, they argued that the prolongation of the atrial ERP played a key factor in the decrease of the AF induction rate in those patients ablated by surgical cryoablation. Probably, the larger myocardial injury created by surgical cryoablation or dissection of the atrioventricular sulcus may be related to the lower incidence of AF. Another factor that might have influenced is that the radiofrequency applications were mainly delivered on the ventricular side of the atrioventricular valve annulus, whereas surgical cryoablations were performed directly on the atrial tissue. Therefore, the injury of the atrial tissue was greater in this latter group of patients. The resulting prolongation of the atrial ERP may prevent the capture of short coupled premature atrial excitation and, therefore, may result in the prevention of atrial electrical disorganization and AF.

Atrial electrophysiological responses induced by programmed stimulation

There are several atrial electrophysiological parameters relating to AF which are elicited with atrial programmed...
The inducibility of AF, fragmented atrial activity, repetitive atrial firing, and intra-atrial conduction delay have been previously examined. Transient AF was induced in 83% of the WPW patients with a history of clinically documented PAF. To clearly assess the intrinsic atrial vulnerability in WPW patients is necessary to perform a complete electrophysiological study before and after AP ablation. Hamada et al. studied the existing electrophysiological differences between WPW patients whose AF remained inducible, and those with AF that could not be induced following AP ablation. They demonstrated that WPW patients with AF had significantly longer maximal atrial conduction delay and wider conduction delay zone than controls. Considering only the patients with WPW syndrome and AF, ablation of the AP did not change the maximal atrial conduction delay and conduction delay zone in those patients whose AF remained inducible. However, AP ablation normalized the maximal atrial conduction delay and conduction delay zone in those patients whose AF remained non-inducible. Therefore, they suggest that there is a definitive electrophysiological evidence of two different mechanisms for AF in the WPW syndrome; one is reversible and AP-dependent atrial vulnerability and the other is intrinsic and AP-independent atrial vulnerability.

AF can also be initiated by ectopic beats originating from the pulmonary veins and elsewhere. The pulmonary veins are well established as the dominant sources of triggers in PAF, in addition to their contribution to maintenance of AF. However, there is no available data suggesting that firing from the pulmonary veins is the main source of recurrent AF in WPW patients that had their AP ablated. The elimination of triggers of AF requires spontaneous firing to be readily identifiable during an ablation procedure. Ablation targeting the pulmonary vein–left atrial junction is effective in isolating the left atrium from proarrhythmic pulmonary vein activity. Despite the latest progress in AF ablation, there is limited knowledge of how to identify, map, and ablate the culprit atrial substrate in an individual patient, because AF is generally associated with locally complex electrograms of indefinite timing and sequence. This heterogeneity of substrate may explain why no single predetermined ablation technique is effective for all patients across the entire spectrum of AF. To the best of our knowledge, there is no detailed study addressing ablation of the pulmonary veins to suppress recurrent AF in WPW patients that had already undergone successful AP ablation.

**Fragmented atrial activity**

A single atrial extrastimulus delivered with a critical coupling interval often results in widening of the local atrial electrogram. The mechanism producing fragmented atrial activity is not clear. Fragmentation of the atrial electrogram in response to premature stimulation has been demonstrated in several experimental and clinical studies. Fragmented atrial activity might represent local continuous activity in response to premature beats. Ohe et al. defined it as the occurrence of disorganized atrial activity ≥150% of the duration of the local atrial electrogram of the basic beat recorded in the high right atrium. It has been demonstrated that fragmentation and slowing of conduction in response to premature stimulation are related to PAF. Although fragmented atrial activity is also elicited in subjects without PAF, the widening of fragmented atrial activity zone is characteristic of PAF. Patients with WPW syndrome associated with PAF have a wider fragmented atrial activity zone than those WPW patients without PAF. This suggests that the widening of the fragmented atrial activity zone is closely related to the occurrence of AF in patients with WPW syndrome.

**Atrial conduction delay**

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 to develop. Inter-atrial conduction delay, measured from the stimulus artefact to the atrial electrogram at the distal coronary sinus level, reflects an actual inter-atrial conduction delay that is not influenced by local latency at the site of stimulation, since the stimulation is performed in the high right atrium. Shimizu et al. defined inter-atrial conduction delay as an increase in the S2 through A2 interval of the extrastimulus >20 ms compared with the S1 through A1 of the basic drive (Figure 3). Aytemir et al. demonstrated a significant increased in the maximum P wave duration and P wave dispersion after AP ablation reflecting more inhomogeneous and prolonged atrial conduction times in patients with the WPW syndrome and PAF episodes. Therefore, this increased P max and higher P wave dispersion values in patients with previous PAF episodes suggest the important role of inhomogenous and discontinuous atrial propagation of sinus impulses in the development of AF in patients with the WPW syndrome. They demonstrated that the maximum P wave duration and...
P wave dispersion are independent predictors of recurrence of PAF in patients with the WPW syndrome after successful radiofrequency catheter ablation. Hiraki et al. demonstrated in a prospective study that P wave signal-averaged electrocardiography predicts recurrence of PAF in patients with WPW syndrome who underwent successful catheter ablation. To reduce inter-atrial conduction delay and decrease atrial vulnerability, bi-atrial pacing was developed as a technique of simultaneous activation of the right atrium; RAA, right atrial appendage; HBE, His bundle area; and Csd, distal coronary sinus. Reprinted with permission from Isomoto et al.  

Repellent atrial firing  

Several clinical studies have demonstrated that repetitive atrial firing is a common finding in patients with PAF. According to Wyndham et al., repetitive atrial firing 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 (Figure 4). Patients with AF demonstrated a higher incidence of repetitive atrial firing and a significantly wider repetitive atrial firing zone than did the control subjects, suggesting the existence of a common electrophysiological mechanism in both PAF and repetitive atrial firing. Shimizu et al. observed that the atrial ERP was significantly shorter at sites where repetitive atrial firing was induced than at sites where it was not induced. Repellent atrial firing reportedly occurred in 94% of the atrial sites with an ERP of 260 ms and a maximum conduction delay >40 ms. These results suggest that the occurrence of repetitive atrial firing requires the presence of a short refractory period at the pacing site and prolongation of the maximum conduction delay. It was shown that WPW patients associated with PAF have a wider repetitive atrial firing zone than those WPW patients without PAF. This suggests that the patients with PAF would have a greater tendency to develop repetitive atrial firings in response to an atrial premature contraction in the setting of WPW syndrome.

Abnormal atrial endocardial electrograms in sinus rhythm  

At the time of atrial endocardial mapping during sinus rhythm, the recording of an abnormally prolonged and fractionated right atrial electrogram may reflect slow and anisotropic conduction through a diseased atrial muscle. Tanigawa et al. made the first attempt to define quantitative characteristics of normal atrial endocardial electrograms with a catheter electrode mapping technique of the right atrium during sinus rhythm (Figure 5A). They recorded atrial endocardial electrograms from the anterior, lateral, posterior, and medial aspects of the high, middle, and low right atrium. The duration of the atrial electrograms was defined as the time from the beginning of the earliest electrical activity that deviated from the stable baseline to the last point of the atrial electrogram that crossed the baseline. The number of fragmented deflections was measured by counting the number of downward deflections. An abnormal atrial electrogram was defined as having a duration >100 ms and eight or more fragmented deflections (Figure 5B). The sites where this kind of activity is recorded may indicate reentry circuit sites. It has been shown in experimental studies that fractionated electrograms are because of asynchronous activation of myocardial fibres at a recording site where connective tissue separates the myocardial fibres, decreasing their interconnections and distorting their orientation. These suggest that the fractionated and prolonged atrial electrograms may indicate the presence of areas that possibly predispose the occurrence of reentry. AF is associated to fibrodegenerative changes in the atrial muscle according to documented pathological studies. It was clearly demonstrated in histopathological studies that those patients who develop AF have an
evident, diffuse, and extensive alteration in the atrial histology compared with those who do not develop AF. The histological studies of the atrial tissue that had electrophysiological alteration consist of widely separated atrial fibres and distorted by connective tissue, which results in a decreased intercellular connexions and thus, an increased flow current resistance and slow conduction. In a pathological study of fatal cases with WPW syndrome and sudden cardiac death, Basso et al. observed a 50% incidence of isolated atrial myocarditis. Sudden death was the first manifestation of the disease in 40% of the cases. This finding of atrial inflammatory infiltrates in patients with the WPW syndrome supports the hypothesis that atrial inflammatory foci may act as a trigger of PAF, which in turn precipitates sudden cardiac death because of very rapid ventricular conduction.

Abnormally prolonged and fractionated atrial electrograms were frequently (83%) recorded in WPW patients associated with PAF. However, these abnormal atrial electrograms were significantly less common (10%) in WPW patients without any evidence of PAF. These electrophysiological abnormalities of the atrial muscle were more frequently and significantly found in the high right atrial sites distant from the atrioventricular groove and AP location. Since abnormally prolonged and fractionated atrial electrograms were also frequently found in patients with PAF not associated to the WPW syndrome, it is suggested that the mechanism of abnormal atrial electrograms may not relate to the AP. Therefore, patients with the WPW syndrome associated with PAF have a significantly high incidence of electrophysiological abnormalities of the atrial muscle which certainly play an important role in the occurrence of AF in these patients.

Conclusions

Atrial fibrillation has a particular prognostic significance in patients with the WPW syndrome, and its incidence is unusually high in the absence of any clinical evidence of organic heart disease. It may be life-threatening if an extremely rapid ventricular response develops degenerating into ventricular fibrillation. The existence of a retrograde multiple or multifibre AP is strongly related to AF inducibility, and the complex excitation inputs into the atrium over the retrograde multiple or multifibre AP facilitate the development of AF in WPW patients. The decrease incidence of PAF after successful elimination of the AP suggests that the AP itself may play an important role in the initiation of PAF.

On the other hand, there is an important evidence of an underlying atrial disease in patients with the WPW syndrome. Abnormally prolonged and fractionated atrial endocardial electrograms are observed with a significantly higher incidence in WPW patients with documented episodes of AF. Furthermore, the electrophysiological findings of altered atrial refractoriness, increased induction of repetitive atrial firing and increased intra-atrial conduction delay suggest an intrinsic atrial vulnerability as the mechanism of PAF in certain patients with the WPW syndrome. The atrial vulnerability in the WPW syndrome seems to be either reversible and AP-dependent, or intrinsic and AP-independent atrial vulnerability.

Therefore, it is concluded that the available evidence suggests the presence of different mechanisms of AF development in different patients with the WPW syndrome. A detailed electrophysiological examination before and after AP ablation could shed insight into the understanding of the mechanism for the genesis of AF in individual patients with the WPW syndrome.
Conflict of interest: none declared.

References


