

Predictors of the atrial fibrillation occurrence in patients with Wolff-Parkinson-White syndrome

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Abstract

Background: Atrial fibrillation (AF) in WPW syndrome occurs earlier and is more common than in the general population.

Aim: To evaluate the predisposing factors for the first episode of AF in patients with WPW.

Methods: We analysed data on 930 patients (510 males, 420 females) with WPW treated in our centre during 1988-2007. AF was diagnosed in 236 patients (25% – 161 males, 75 females, aged 36 ± 15 years). The AF group was divided into two subgroups – patients with AF and atrio-ventricular reentrant tachycardia (AVRT), and patients with AF only. The analysis included subjects' age and gender, the presence of AVRT, the number and properties of accessory pathways, left ventricular ejection fraction (LVEF) and concomitant cardiovascular diseases.

Results: The groups did not differ in terms of concomitant diseases and LVEF. In the whole group of patients with AF, arrhythmia occurred earlier in men than in women (34 ± 14 vs. 40 ± 15 years of age, $p = 0.013$). In the subgroup with AF and AVRT, AF was documented earlier compared to patients with AF only (34 ± 15 vs. 41 ± 15 years of age, $p = 0.0072$). AVRT was more common in patients with AF compared to those without AF (69 vs. 53%, $p < 0.001$). In the whole group of 930 patients, AF was observed more often in patients with overt pre-excitation compared to concealed WPW (29 vs. 12%, $p < 0.001$).

Conclusions: In patients with WPW syndrome, AF occurs earlier in patients with AVRT compared to patients with AF and without documented AVRT, earlier in men compared to women, and is more common in patients with overt WPW.

Key words: atrial fibrillation, Wolff-Parkinson-White syndrome, atrioventricular tachycardia

Kardiologia Polska 2009; 67: 973-978

Introduction

Paroxysms of atrial fibrillation (AF) in Wolff-Parkinson-White (WPW) syndrome occur earlier and are more common than in the general population [1]. In 1941 Levine and Beeson [2] described patients with features of pre-excitation, who had 'irregular' tachycardia with wide QRS complexes. These were probably patients with WPW syndrome and paroxysms of AF.

There are many hypotheses attempting to explain the frequent occurrence of AF in the WPW syndrome. Analysis of atrial pressures during atrioventricular tachycardia (AVRT) demonstrated significantly higher pressure values in patients who suffered from paroxysms of AF. Higher pressures in patients with AF are a consequence of different characteristics of a tachycardia loop determined by the properties of an accessory pathway (AP), atrioventricular node or atrial and ventricular muscle. Atrial stretching may lead to atrial cardiomyopathy and increased

susceptibility to AF. In this situation AVRT can more easily degenerate to AF [3].

Some authors suggest that atrial architecture and increased atrial vulnerability may be influenced by the morphology of the AP insertions [4], and that anisotropic features of left-sided oblique AP are caused by the connection between the ventricular muscle and the coronary sinus (ventricular insertion) and between the coronary sinus and the atrial muscle (atrial insertion) [5].

Long interatrial conduction time, short atrial effective refractory period as well as P wave dispersion occur significantly more frequently in patients with WPW and paroxysms of AF [6]. Marked reduction (76 to 91%) of the occurrence of AF paroxysms after ablation confirms the important role of AP in triggering AF [7, 8].

In patients with overt WPW syndrome ventricular rhythm during AF is determined mainly by the AP refractory period, but it is also dependent on the refractory period and conduction velocity in the atrioventricular node, as

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Received: 27 January 2009. Accepted: 06 July 2009.

well as on the atrial and ventricular muscle characteristics and the degree of sympathetic system activity [9]. If AP has a short effective refractory period (ERP) AF leads to extremely fast ventricular rhythm and, in some patients, to ventricular fibrillation and death [10, 11].

Patients with WPW have class I and evidence level B indication for ablation [12]. Patients with features of pre-excitation, without paroxysms of arrhythmia, and patients without features of pre-excitation with single or sporadic paroxysms of AVRT have an indication for ablation of class IIa, evidence level B.

The aim of the study was to assess the onset and predictors of the first AF paroxysm occurrence in patients with WPW syndrome.

Methods

The analysis included gender, type of WPW (overt, intermittent, concealed), presence of AVRT, number of APs and concomitant diseases. Patients had a physical examination and their medical history, available ECG and Holter ECG registrations as well as laboratory findings were analysed. Coronary angiography was performed in sixty patients (25%) with a probability of coronary artery disease.

All patients underwent electrophysiological study (EPS). Only one extra stimulus was used for programmed stimulation to minimise the risk of AF induction and to assess the susceptibility to arrhythmia in patients with or without documented AF.

Study group

Data on 930 patients with WPW subjected to non-pharmacological treatment (surgery or RF ablation) in the

Institute of Cardiology between 1988 and 2007 were analysed (510 men, 420 women). Paroxysmal AF was present in 236 (25%) patients (161 men, 75 women; 6-75 years of age, mean 36.4 ± 15). Coronary artery disease was found in 7% of patients, hypertension (HT) in 20%, valvular heart disease (VHD) in 8%, mitral valve prolapse (MVP) with minimal or mild insufficiency in 22%. Left ventricular ejection fraction (EF) and fractional shortening (FS) were normal in 99% of cases (respectively 64 ± 10 and 37 ± 6). Two patients had $EF < 50\%$.

Patients with AF were divided into 2 subgroups: group 1 – those with coexisting paroxysms of AVRT and AF; group 2 – those with paroxysms of AF only.

Statistical analysis

Results are presented as means \pm SD or numbers and percentages. Results were compared using nonparametric tests. Nonparametric NPAR1WAY procedure (SAS) was applied to verify the hypothesis regarding age; age distribution in the study group made it impossible to use parametric tests (the hypothesis of normal distribution was rejected with $p = 0.001$). Values of $p < 0.05$ were considered statistically significant.

Results

Patients from the two groups did not differ in terms of concomitant diseases, as well as EF and SF. In the group of 236 patients with AF, the first paroxysm of AF occurred most frequently in the fourth decade of life (24%). After adjustment for sex, the first episode of AF occurred earlier in men than in women, in the third (26%) and the fourth decade (25%), respectively (Figure 1).

Documented arrhythmias and the first paroxysm of AF

Both AVRT and AF were documented in 162 patients (56 men, 106 women) (group 1). Two or more paroxysms of AF occurred in 89 of them (38%). Paroxysms of AF relapsed persistently in 40 patients and a focal type of AF had been diagnosed in 6 patients who underwent successful pulmonary vein isolation. Paroxysms of AF occurred in 66 patients (30%) despite amiodarone treatment and hyperthyroidism was diagnosed in 10 of them (30%) as a consequence of amiodarone administration. Forty-four patients underwent direct current cardioversion.

Isolated paroxysms of AF (group 2) were found in 74 patients (16 women, 58 men).

Gender and the first paroxysm of AF

In the whole AF group, first episode of AF occurred significantly earlier in men than in women (34.5 ± 14.5 vs. 40.4 ± 15 years, $p = 0.013$). In group 1 the first paroxysm of AF occurred most frequently in the 4th decade (22%):

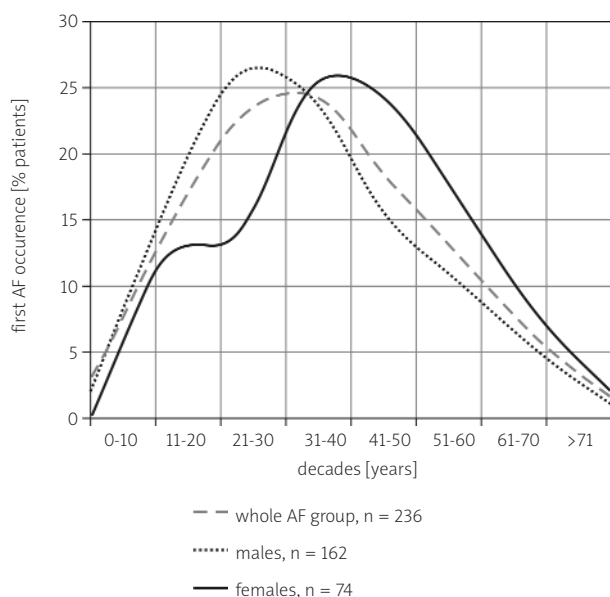


Figure 1. Age of the first AF occurrence in decades in patients with WPW

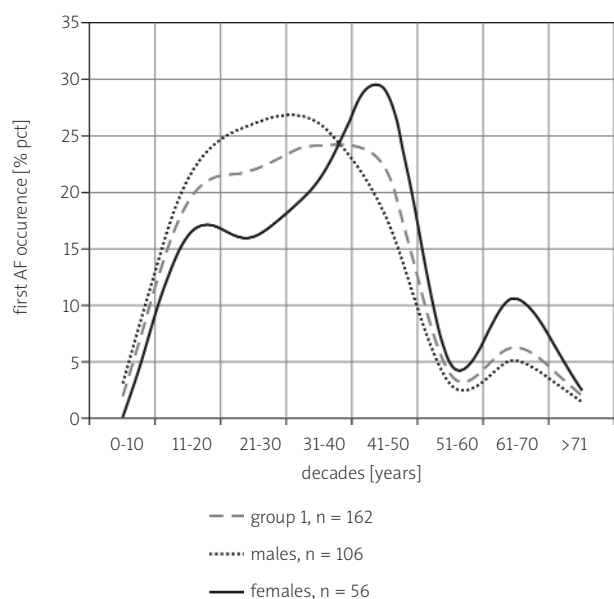


Figure 2. Age of the first AF occurrence in decades in patients from group 1 (AVRT and AF)

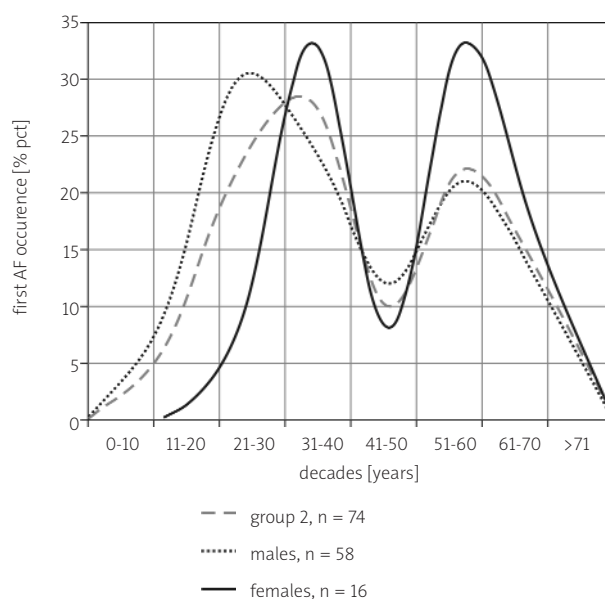


Figure 3. Age of the first AF occurrence in decades in patients from group 2 (AF)

in the 5th decade in women (29%) and in the 3th and 4th decade in men (26% in each) (Figure 2). In group 2 the first paroxysm of AF occurred most frequently in the 4th decade (28%), but earlier in men – in the 3rd decade (30%). Two marked peaks of AF occurrence were observed – first in the 4th and second in the 6th decade (33%) (Figure 3).

Atrioventricular tachycardia and the first paroxysm of AF

In group 1 the first paroxysm of AVRT occurred at 21 ± 14 years of age. The first paroxysm of AF was documented earlier in patients from group 1 than in patients from group 2 (34.3 ± 15 vs. 41 ± 15 , $p = 0.0072$) (Table I). Atrioventricular reentrant tachycardia was present in 69% of patients with AF. The occurrence of AVRT was significantly lower in patients without AF (694) in comparison to those with AF (69 vs. 53%; $p < 0.001$).

There were 1.6 times more women in group 1 than in group 2 (respectively 34.5% and 21.6% – 56/162 vs. 16/74). The 95% confidence interval for the ratio of these fractions

in the studied population was 1.476 and 1.7439. In patients without documented AVRT age distribution of the first AF occurrence had a bimodal character (Figure 3). Two peaks of AF onset were observed – between 20 and 30 years of age and after 50 years of age.

Type of WPW and the first paroxysm of AF

The features of pre-excitation were most frequently overt and permanent (81%) whereas intermittent WPW (11%) or concealed AP (8%) were less frequent. Patients with an overt AP most frequently had the first occurrence of AF in the 4th decade of life (28%) and patients with a transient AP in the 3rd decade (28%). In patients with a concealed pathway AF occurred in the 5th decade of life in 36% of cases (Figure 4).

In the whole group of 930 patients, AF was present significantly more frequently in patients with overt pre-excitation than in patients with concealed WPW (29 vs. 12%; $p < 0.001$) or intermittent pre-excitation (29 vs. 16%; $p < 0.01$).

Table I. Patients' age during the first paroxysm of AF in the analyzed groups

	Number of patients	Age	p
AVRT and AF (group 1) vs. AF (group 2)	162 vs. 74	34.3 ± 15 vs. 41 ± 15	0.0072
Men vs. women	161 vs. 75	34.5 ± 14.5 vs. 40.4 ± 15	0.013
Overt vs. intermittent and concealed	191 vs. 45	37 ± 14 vs. 33 ± 17	0.04
MAP vs. single AP	45 vs. 191	33 ± 12 vs. 36 ± 15	0.4 (NS)

Abbreviations: MAP – multiple accessory pathways, AVRT – atrioventricular tachycardia, AF – atrial fibrillation

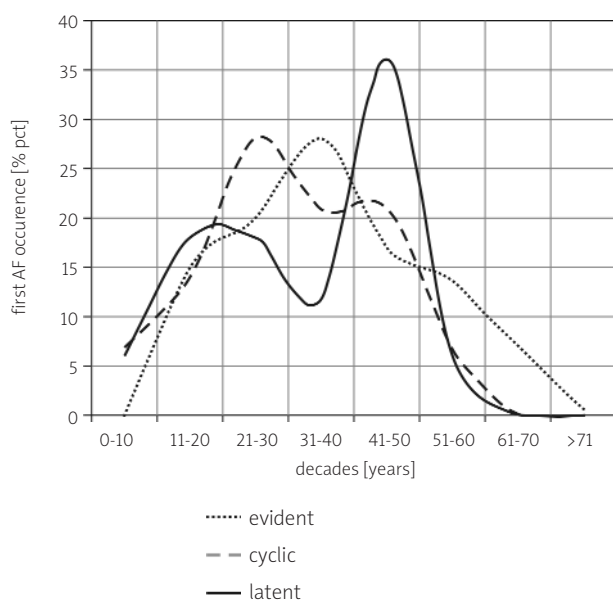


Figure 4. Age of the first AF occurrence in decades in relation to pre-excitation features

Multiple pathways and the age at the first AF

Two APs were present in 45 patients (19%). In those patients AF occurred slightly earlier than in patients with single AP (33 ± 12 vs. 36 ± 15 years, NS). Multiple pathways were more likely present in the AF group than in patients without AF (19 vs. 10%, $p < 0.001$).

Location of the accessory pathway

Patients with AF had most often a left-sided pathway (61%), followed by a right-sided one (30%). A septal pathway was rarely found (9%). In the whole group of 930 patients a left-sided pathway was also the most frequent one, followed by the rarer septal pathway (19%) and the rarest right-sided pathway (15%).

Discussion

The aim of the study was to analyse the time of the first paroxysm of AF in patients with WPW syndrome. There are no reports in literature addressing this issue in a large group of patients. The percentage of patients with paroxysms of AF in our population reached 25%, which is similar to the percentage reported by other authors [5, 13].

Documented AVRT and the first paroxysm of AF

Atrio-ventricular reentrant tachycardia is a known trigger of AF [3, 14]. In our group of patients with paroxysms of AVRT and AF, the first paroxysm of AF occurred earlier than in patients with isolated AF paroxysms. AVRT also occurs more frequently in patients with AF in comparison to patients without AF. This is in line with the theory about a significant influence of AVRT on AF in patients with WPW. It may confirm the theory

that AVRT, by generating higher atrial pressures, causes earlier onset of atrial cardiomyopathy and earlier occurrence of AF [3].

It seems, however, that this is not the only mechanism leading to AF, because there is a large group of patients without paroxysms of AVRT or with paroxysms of AVRT occurring so rarely that they cannot lead to atrial cardiomyopathy. In this group there was a bimodal distribution of the first AF occurrence. Peaks of AF occurrence were at approximately 25 and 50 years of age. It seems that adrenergic stimulation and exercise are the dominating factors during the first peak, while diseases increasing the risk of AF occurrence such as hypertension or coronary artery disease intervene during the second peak.

A syndrome of persistently recurrent focal, atrial arrhythmias was documented in 6 patients with successful ablation of the accessory pathway in the second group. These patients underwent targeted PV isolation and/or Marshall LoM ligament ablation which were responsible for the paroxysms. Because of a documented typical atrial flutter, an ablation line in the cavo-tricuspid isthmus was also performed in this group.

Gender and the first paroxysm of AF

In our group, AF occurred significantly earlier in men than in women. Male gender is one of the independent risk factors of AF occurrence in the published reports [15]. Atrial fibrillation occurred earlier in men and was usually related to strenuous physical exercise or emotions, e.g. when playing sports. It is similar during the first three decades in the whole group of patients with WPW. New predisposing factors and the background for triggering and sustaining AF such as coronary artery disease or hypertension appear in the following decades. These results are in agreement with the work of Schwieler et al. [16], who also observed more frequent occurrence of AF in men.

Type of conduction through an accessory pathway and the first paroxysm of AF

The well known fact of more frequent AF occurrence in patients with WPW is in the opinion of most scientists related to the presence of retrograde conduction through an AP. It should be noted however that patients with overt pre-excitation accessory pathways usually conduct in both antegrade and retrograde directions [17]. This is why in some analyses AF occurs less frequently in patients with concealed WPW syndrome [15, 16].

Multiple accessory pathways and the first paroxysm of AF

Many studies refer to multiple pathways as one of the risk factors of AF occurrence in WPW syndrome [18]. Campbell et al. [1] described the role of retrograde

conduction through multiple APs in the occurrence of atrial premature beats inducing intra-atrial re-entry. We also found a higher incidence of multiple APs in patients with rather than without AF, however, no differences in the patient's age at the first AF episode were noted.

Conclusions

1. The presence of atrioventricular tachycardia predisposes to earlier occurrence of atrial fibrillation paroxysms.
2. Atrial fibrillation, which is a life-threatening arrhythmia, occurs first in men with overt WPW syndrome or with heart palpitations, and these patients should be primarily referred for ablation of an accessory pathway.

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Pierwszy napad migotania przedsionków u chorych z zespołem Wolffa-Parkinsona-White'a

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Streszczenie

Wstęp: Napady migotania przedsionków (AF) w zespole Wolffa-Parkinsona-White'a (WPW) występują wcześniej i z namiennie częściej niż w populacji ogólnej.

Cel: Ocena czasu wystąpienia pierwszego napadu AF u chorych z dodatkowym szlakiem przedsionkowo-komorowym (AP) o szybkim przewodzeniu. W analizie uwzględniono płeć, postać WPW, występowanie częstoskurczu przedsionkowo-komorowego (AVRT), liczbę AP oraz choroby towarzyszące.

Metody: Przeanalizowano dane 930 pacjentów (510 mężczyzn, 420 kobiet) z AP, którzy zostali poddani leczeniu niefarmakologicznemu (operacja, ablacja RF) w Instytucie Kardiologii w latach 1988–2007. Napady AF miało 236 (25%) pacjentów (161 mężczyzn, 75 kobiet; wiek 36 ± 15 lat) i tę grupę poddano szczegółowej analizie. Pacjentów z AF podzielono na 2 grupy: grupa 1 – pacjenci z napadami zarówno AVRT, jak i AF; grupa 2 – pacjenci tylko z napadami AF.

Wyniki: Chorzy z obu grup nie różnili się między sobą pod względem współwystępowania chorób i pod względem frakcji wyrzutowej (EF). W grupie osób z AF arytmia ta występowała wyraźnie wcześniej u mężczyzn (34 ± 14 vs 40 ± 15 lat, $p = 0,013$). U osób z grupy 1 (AF i AVRT) udokumentowano pierwszy napad AF wcześniej niż u chorych z grupy 2 ($34,3 \pm 15$ vs 41 ± 15 lat, $p = 0,0072$). W porównaniu grupy pacjentów z AF z pozostałymi pacjentami (694 osoby) AVRT występował z namiennie częściej u chorych z AF (69 vs 53%, $p < 0,001$). W analizie całej grupy (930 pacjentów) AF występowało z namiennie częściej u osób z jawnymi cechami preekscytacji niż u osób z utajonym zespołem WPW (29 vs 12%, $p < 0,001$).

Wnioski: Obecność AVRT predysponuje do szybszego pojawienia się napadu AF: 1) wyraźnie wcześniej w grupie z napadami AVRT i AF w porównaniu z grupą bez udokumentowanych napadów AVRT, 2) wcześniej u mężczyzn niż u kobiet; oraz 3) częściej w grupie z jawnym zespołem WPW. Migotanie przedsionków, które jest arytmia zagrażającą życiu, pojawia się najwcześniej u mężczyzn z jawnym zespołem WPW oraz z kołataniem serca, dlatego też tych pacjentów powinno się jak najszybciej kierować na ablację szlaku dodatkowego.

Słowa kluczowe: migotanie przedsionków, zespół Wolffa-Parkinsona-White'a, częstoskurcz przedsionkowo-komorowy

Kardiologia Pol 2009; 67: 973-978

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Praca wpłynęła: 27.01.2009. Zaakceptowana do druku: 06.07.2009.