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A comparison of the clinical course of preexcitation syndrome in children and adolescents and in adults

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Abstract

Background: *Atrioventricular reentrant tachycardia (AVRT) in patients with preexcitation syndrome (PS) is the main cause of paroxysmal regular arrhythmias in children and adolescents. While the previously published data most commonly concern clinical consequences of PS in adults, few researchers have evaluated the problem in children and adolescents. The aim of the study was to compare the clinical course of PS between the population of children and adolescents below 19 years of age and the population of adult patients.*

Method: *The study population consisted of 302 consecutive PS patients managed between January 2001 and June 2005 with radiofrequency catheter ablation (RFCA). The study population was divided into two groups: Group 1 consisting of 52 patients aged 15.38 years on average (7–18 ± ± 2.53) and Group 2 consisting of 250 adult patients aged 38.67 years on average (19–72 ± 13.1).*

Results: *Patients from Groups 1 and 2 experienced their first episode of AVRT at the mean age of 13.3 years and 29.1 years, respectively ($p < 0.05$). The mean annual numbers of AVRT episodes in Groups 1 and 2 were 12.97 (range, 2–96; median, 8) and 8.86 (range, 2–25; median, 6), respectively (p = non-significant). Two patients from Group 1 (3.85%) and 42 patients from Group 2 (16.8%) experienced episodes of atrial fibrillation (AF) ($p < 0.05$). Location of the accessory pathways (AP): In Group 1, the right free wall and anteroseptal AP locations were significantly more common [11 (21.15%) and 9 (17.31%) patients, respectively,* vs. *19 (7.6%) and 13 (5.2%) patients in Group 2; $p < 0.01$]. In Group 2, the left anterolateral AP location was more common [81 (32.4%)* vs. *4 (7.69%) in Group 1; $p < 0.01$].*

Conclusions: *In children and adolescents with PS, a significantly lower incidence of AF was found. In Group 1, RFCA was performed significantly more frequently due to the development of AVRT caused by right free wall and right anteroseptal AP, while in the group of adults, the left anterolateral AP location was found more commonly.* (Cardiol J 2007; 14: 384–390)

Key words: preexcitation syndrome, clinical course, children and adolescents

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Introduction

Atrioventricular reentrant tachycardia (AVRT) with an involvement of an accessory pathway (AP) in patients with preexcitation syndrome (PS) is the main cause of reentrant arrhythmias in children and adolescents with structurally healthy hearts.

The formation of the accessory connection is a consequence of abnormal development of the fibrous rings in the heart, which form the anatomic and electric barrier that separates the atria from the ventricles. Developmental anomalies in the embryonic period make it possible for atrial fibres to penetrate the ventricular myocardium. The annual prevalence of PS is 4 per 100,000 persons and it is estimated that electrocardiographic signs of preexcitation may be found in 0.1–0.3% of the general population. In the population of children, the incidence of PS is estimated at approximately 0.1% [1].

The clinical picture of PS may vary from asymptomatic to life-threatening secondary tachyarrhythmias. While the published data most commonly concern clinical consequences of PS in adults, few researchers have evaluated this problem in children and adolescents [2].

The aim of the study was to compare the clinical course of PS between the population of children and adolescents below 19 years of age and the population of adult patients.

Method

The study population consisted of 302 consecutive symptomatic patients with drug-resistant PS without a structural heart disease, managed between January 2001 and June 2005. All the patients underwent the invasive electrophysiologic study (EPS) and radiofrequency catheter ablation (RFCA). The study was conducted after the patient or, in the case of children, the patient's parents or legally acceptable representatives had been informed of the aims, methodology and the possible complications of the procedure and after informed consent had been obtained. The study population was divided into two groups: Group 1 consisting of 52 patients less than 19 years of age and Group 2 consisting of 250 adult patients.

A retrospective analysis of the following parameters describing the course of the disease were evaluated: duration of symptoms in the form of paroxysmal tachyarrhythmias, annual frequency of tachycardia episodes, presence of clinically documented episodes of atrial fibrillation (AF) or flutter and syncopes, and a history of episodes of cardiac arrest. A comparative analysis of locations of the accessory pathways was also performed.

We used the classification of accessory pathways developed by Josephson, who distinguished the following AP locations: right free wall (RFW), right anteroseptal (RAS), right mid-septal (RMS), right posteroseptal (RPS), left posteroseptal (LPS), left posterolateral (LPL) and left anterolateral (LAL) [3]. In addition, pathways which end in the coronary sinus were distinguished (CS).

Subjects in whom the presence of more than one accessory pathway was discovered were classified to all AP location groups. Example: a patient with two accessory pathways, left posteroseptal and left posterolateral was included in two groups of AP location: LPS and LPL. Hence the number of AP in Table 1 is higher than the number of subjects.

Statistical analysis

The comparative analysis of continuous variables between the groups was performed using the t-Student test for unpaired data. The significance of the differences for qualitative variables was tested using the non-parametric χ^2 test with Yates' correction for small sample sizes.

Table 1. Comparative analysis of the clinical course of preexcitation syndrome.

	Group 1	Group 2	P value
Mean age (SD) at onset of symptoms	13.33 (1.73)	29.12 (12.27)	< 0.001
Annual number of atrioventricular reentrant tachycardia episodes	12.97 ±16.5 (2–96) median 8	8.86 ± 8.07 (2–52) median 6	NS
Cardiac arrest	1 (1.92%)	5 (2.0%)	NS
MAS	0	7 (2.8%)	NS
Atrial fibrillation	2 (3.85%)	42 (16.8%)	< 0.05
Atrial flutter	0	9 (3.6%)	NS

Table 2. Demographic and clinical characteristics of both study groups.

	Group 1	Group 2	P value
Number of patients	52	250	NS
Sex (female)	24 (46.15%)	115 (46%)	NS
Mean age (SD)/range [years]	15.38 (2.53)/7–18	38.67 (13.1)/19–72	< 0.05
Mean LVEDD (SD)/range [mm]	45.69 (5.05)/39–54	48.83 (6.24)/35–67	NS
Mean LVESD (SD)/range [mm]	29.23 (4.58)/23–38	30.63 (5.06)/22–44	NS
Mean LVEF (SD)/range (%)	64.92 (4.42)/60–72	55.58 (6.52)/35–75	NS

LVEDD — left ventricular end-diastolic dimension in the parasternal view, M mode; LVESD — left ventricular end-systolic dimension; LVEF — left ventricular ejection fraction in the apical four-chamber view

Results

Demographic and clinical characteristics of both groups

Group 1 consisted of 52 patients aged 15.38 years on average, in whom electrophysiologic studies revealed signs of preexcitation and/or AVRT was induced. The adult group consisted of 250 patients aged 38.67 years on average. In Group 2, ischemic heart disease was present in 10 patients (4%), hypertension in 30 (12%) and type 2 diabetes in 1 (0.4%); 4 patients (1.6%) had a history of myocardial infarction (Table 2).

In the group of children and adolescents, the mean age at first episode of tachycardia was 13.3 years and was significantly lower than in the group of adults (29.1 years, $p < 0.05$). The mean annual numbers of AVRT episodes in Groups 1 and 2 were 12.97 (range, 2–96; median, 8) and 8.86 (range, 2–25; median, 6), respectively (p = non-significant). One patient (1.92%) from Group 1 and 5 (2.0%) from Group 2 had suffered an episode of cardiac arrest (p = non-significant). Analysis of the history of syncope episodes revealed no patients with a history of MAS episodes in Group 1 and 7 patients (2.8%) a history of MAS episodes in Group 2 (p = non-significant). In group 1, significantly fewer patients had experienced documented clinical episodes of AF [2 (3.85%) *vs*. 42 (16.8%), $p < 0.05$]. There were no documented cases of atrial flutter in Group 1, while 9 patients (3.6%) from Group 2 had experienced episodes of atrial flutter (p = non-significant) (Table 1).

Location of the accessory pathway

In Group 1, the right free wall and anteroseptal AP locations were significantly more common [11 (21.15%) and 9 (17.31%) patients, respectively, *vs*. 19 (7.6%) and 13 (5.2%) patients in Group 2; $p < 0.01$], while in Group 2, the most common AP location was left anterolateral [81 (32.4%) *vs*. 4 (7.69%) in Group 1, $p < 0.01$]. The distribution of the other AP locations, including the occurrence of multiple APs was similar in both groups of patients (Table 3).

Discussion

Paroxysmal regular tachycardias with narrow QRS complexes are the most common tachyarrhythmias in children and adolescents with

Table 3. Comparative analysis of the accessory pathway locations.

Accessory pathway location	Group 1	Group 2	P value
Right free wall	11 (21.15%)	19 (7.60%)	< 0.01
Right anteroseptal	9 (17.31%)	13 (5.20%)	< 0.01
Right mid-septal	3 (5.77%)	28 (11.20%)	NS
Right posteroseptal	8 (15.38%)	28 (11.20%)	NS
Coronary sinus	2 (3.85%)	26 (10.40%)	NS
Left posteroseptal	4 (7.69%)	20 (8.0%)	NS
Left posterolateral	13 (25.0%)	54 (21.60%)	NS
Left anterolateral	4 (7.69%)	81 (32.40%)	< 0.01
MAP	2 (3.85%)	20 (8.0%)	NS
AP ERP [ms] mean ±SD/range	246.88 ± 9.46/230–260	253.81 ± 13.37/230–280	NS

AP ERP — accessory pathway effective refraction period

structurally healthy hearts. In this age group, approximately 70% of the diagnosed cases were caused by atrioventricular reentrant tachycardia due to the presence of an accessory pathway [2]. The course of the disease in children and adults can vary and ranges from asymptomatic to life-threatening secondary tachyarrhythmias. Assessment of the risk of adverse consequences of preexcitation syndrome in children is therefore essential to the selection of treatment.

Medical history of the children and adolescents we studied revealed a higher incidence of AVRT episodes than in the group of adult subjects. The mean number of episodes was approximately 13 and 9 in Groups 1 and 2, respectively, although the difference was not statistically significant. One should, however, bear it in mind that the assessment focused on the year preceding RFCA only. Documented episodes of atrial fibrillation were, however, experienced by a significantly lower number of patients in Group 1 versus Group 2 (3.85% *vs*. 16.8%).

In the literature, the role of the mere presence of an accessory pathway in the induction of paroxysmal atrial fibrillation is emphasised. Some patients are suspected to have heterogenous and bifurcated ends of the AP, which allows for the generation of microreentry waves as a result of changes in electrophysiologic parameters in this area [4]. Arguments to the contrary are provided by Fujimura et al. [5], who found that atrial fibrillation was initiated by rapid atrial tachycardia which started at a high right atrial site and generated into the AF within 10 to 20 cycles. There are also reports which emphasise adrenergic predominance and reduced parasympathetic activity in patients with AF and preexcitation syndrome, which may result in shorter AP refraction periods and shorter cycle of tachycardia [6]. In a postmortem study of patients with documented preexcitation syndrome who had died of sudden cardiac death (SCD), Basso et al. [7] found local inflammation in the atria in 50% of the subjects, which could have been the source of rapid electric activity. There are also reports of effects of temporal sequence of ventricular and atrial activation during AVRT, which may increase atrial pressures [8]. In numerous publications, the prevalence of AF in adults with preexcitation syndrome is estimated at over 30%, while there are few reports on children with PS [9–11]. In the general population of children and adolescents with structurally healthy hearts, AF is extremely rare. Idiopathic AF may develop during pubescence. The presence of an ectopic focus in the pulmonary veins, the crista terminalis or the left atrium is the reported mechanism of induction and maintenance of AF in children and adults without an accessory pathway [1, 12, 13]. Fan et al. [14] found AF during EPS more frequently in patients over 50 years of age than in patients below 30 years of age. The mechanism of this phenomenon is unclear. It may result from the fact that in the general population, the frequency of AF episodes increases with age and changes caused by the presence of an accessory pathway and tachycardia are augmented by degenerative changes causing dispersion of the refraction periods in the atrial myocardium [11]. Lee et al. [15] induced AF during rapid atrial stimulation in 22% of children with preexcitation syndrome, in whom a significantly shorter atrial effective refraction period was found than in the group of children with AVRT without atrial fibrillation.

In the population of adults with preexcitation syndrome, episodes of AF with rapid ventricular response and syncope are regarded as risk factors for SCD, while the risk of SCD in children with the disorder remains unclear [9, 10, 16]. Bromberg et al. [17] investigated 60 patients below 19 years of age with symptomatic WPW syndrome and distinguished three SCD risk groups: high-risk patients with a history of ventricular fibrillation or asystole episode, intermediate-risk patients with a history of AF and syncope and low-risk patients with reentrant tachycardia being the only documented arrhythmia. When RR intervals during induced AF were analysed, values below 220 ms were found in all the patients from the first group, in 74% of the patients in the second group and only in 35% of the patients in the third group.

No statistically significant differences in the accessory pathway effective refraction periods between the three groups were found. The groups did not differ in terms of age, duration of symptoms or coexistence of congenital heart disease [17]. The predictive value of a short RR interval in the assessment of risk for SCD has also been confirmed in studies of adult populations [9, 16].

In a population of children with PS, Dubin et al. [18] compared asymptomatic patients with a group with documented reentrant tachycardias and with patients with a history of syncope episodes. Having analysed the risk factors for SCD that are well established for the adult population (accessory pathway effective refraction < 270 ms, presence of multiple or septal pathways and the possibility of AVRT stimulation), he found no significant differences between the groups.

Few publications indicate that cardiac arrest in the course of AF may be the first manifestation

of preexcitation syndrome, also in the pediatric population [19]. While it seems obvious that children with symptomatic PS, especially drug-resistant, should undergo invasive treatment, no consensus has been reached as to the management of patients in whom electrocardiographic signs of preexcitation are the only manifestation of the disease. Pappone performed a Holter study in a population of 27 asymptomatic children with overt preexcitation syndrome 12 years of age or younger, in whom AVRT or AF were induced during electrophysiologic study.

In this group, episodes of asymptomatic AF with rapid ventricular response were induced in 5 children, while ventricular fibrillation was induced in another two. One patient died a sudden death. In the control group of 105 patients, in whom no reentrant tachycardia or AF could be induced during electrophysiologic study, symptomatic episodes of reentrant tachycardia were recorded in 6 patients, while AF was recorded in 2 patients [20]. Sarubbi et al. [21] performed an invasive electrophysiologic study. In 36 of 62 (58.1%) asymptomatic patients with preexcitation syndrome aged 9.8 ± 5.1 years on average, episodes of supraventricular tachycardia were stimulated, nine of which were episodes of atrial fibrillation. According to the above studies, children with signs of preexcitation on standard electrocardiogram as the only manifestation of the disease are also at risk of sudden cardiac death. In a survey conducted by Campbell et al. [22], most electrophysiologists confirmed that they would perform electrophysiologic study and RFCA in asymptomatic children with overt PS. One should also consider the fact that even very rapid tachyarrhythmias in children with structurally healthy hearts may be oligosymptomatic and that history taking and evaluation of clinical symptoms, especially in younger children, are difficult.

Evaluation of the accessory pathway location in both age groups revealed a significantly higher percentage of right-sided locations (RFW and RAS) and a lower percentage of left anterolateral location in children versus adults. The most likely reason may be the earlier manifestation of tachyarrhythmias dependent on the right-sided location of the accessory pathway.

Fan et al. [14] compared a group below 30 years of age with a group over 50 years of age in terms of the clinical course and found a higher percentage of right lateral accessory pathways in the younger group (14% *vs*. 2%). Tada et al. [23] analysed 910 patients with preexcitation syndrome and found a statistically significant younger age of onset of symptoms in the form paroxysmal tachycardias in patients with right-sided versus left-sided locations of AP (21 ± 12 years *vs*. 23 ± 15 years). Factors contributing to the earlier manifestation of tachyarrhythmias dependent on the right-sided accessory pathways have not been completely elucidated. The most common mechanism that initiates tachycardia in preexcitation syndrome is atrial premature beat arising in close vicinity of the atrial end of the accessory pathway. Hence the greater tendency of the right atrium to generating premature beats may result in the earlier manifestation of reentrant atrioventricular arrhythmias dependent on right-sided pathways. Another condition for the maintenance of tachycardia includes an appropriate relationship of refraction periods and conduction velocity between the accessory pathway, atrioventricular junction and atrial and ventricular myocardium [14]. Liu et al. [24] observed a longer RR interval with right-sided versus left-sided and septal AP locations in patients with preexcitation syndrome. In addition, in the group of patients with a right-sided accessory pathway, they found first degree atrioventricular block with a PR of > 220 ms. The prolongation of conduction through the His-Purkinje system may offer sufficiently long time to end the refraction period in the accessory pathway and to develop a reentry loop. Contrasting results were obtained by Perry and Garson [25] in a population of 140 children, they found no differences in the clinical course of the disease that would depend on the accessory pathway location, including the age of onset of AVRT. In our population, during electrophysiologic study of patients below 19 years of age, AP refraction period was assessed in 25 patients (48.08%) versus 134 adult patients (53.6%). The values did not differ significantly between the groups. The mean retrograde effective refraction period of the AP was 246.88 ms in Group 1 and 253.81 ms in Group 2. Evaluation of refraction periods in Group 1 is most probably inadequate due to the fact that in the majority of patients, the procedure was performed under general anesthesia.

In Group 1, we found multiple accessory pathways in 2 patients (3.85%), which was not significant in comparison to the 8% of MAP in the adult population. In published studies, the frequency of multiple pathways is estimated at 3–22% [26]. The slightly lower frequency of more than one AP in Group 1 in our study may result from the exclusion of patients with structural heart anomalies. Weng et al. [27] found multiple (2 to 4) accessory pathways in 28 of 317 children with preexcitation syndrome. In this

group, they noted a higher percentage of patients with a coexistent structural heart disease (Ebstein syndrome — 3, L-transposition of large vessels — 1, hypertrophic cardiomyopathy — 1).

Clinical implications

In children and adolescents with preexcitation syndrome, a significantly lower incidence of dangerous complications in the form of atrial fibrillation was found compared to adults.

In the younger group, RFCA was performed significantly more frequently due to the development of AVRT caused by right free wall and right anteroseptal accessory pathways, while in the group of adults, the left anterolateral accessory pathway location was found more commonly.

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