

Follow-up of 134 Pediatric Patients with Wolff-Parkinson-White Pattern: Natural Outcome and Medical Treatment

AMALIA N. STEFANI, GABRIELA R. DAL FABBRO, MARÍA J. BOSALEH, ROBERTH VÁSQUEZ, GUSTAVO A. COSTA, RICARDO SPERANZA, JORGE L. GENTILE, CLAUDIO DE ZULOAGA^{MTSAC}

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Address for reprints:

Amalia N. Stefani
Almafuerte 1722
(1650) San Martín,
Pcia. de Buenos Aires
e-mail: amaliastefani@hotmail.com

ABSTRACT

Objective

The aim of the study was to evaluate the outcome of a pediatric population with ventricular pre-excitation pattern, supraventricular tachycardia, atrial fibrillation, cardiomyopathies, mortality and medical treatment.

Methods

From 1976 to 2011, a descriptive observational study was conducted on patients with ventricular pre-excitation in the electrocardiogram. All patients underwent an echocardiogram, 101(75.3%) Holter monitoring, and 69 (51.5%) an ergometric test. Radiofrequency ablation was performed in selected patients. Data were expressed as mean and standard deviation.

Results

The study population consisted of 134 patients; 80 (59.7%) were male. Age at diagnosis ranged from 2 days to 18 years (mean 6.5 ± 5 years). Clinical follow-up lasted 1 month to 20 years (mean 3.6 ± 3.9 years). Thirty five patients (26.1%) consulted for supraventricular tachycardia, 16 (11.9%) for ventricular pre-excitation, and the remaining 83 patients (61.9%) for other abnormalities. Seventy-six patients (56.7%) had left conduction pathway and 3 patients double conduction pathway. Sixteen patients (11.9%) presented supraventricular tachycardia during follow-up. Overall, 51 patients (38%) had orthodromic tachycardia at 6.3 ± 5.8 years, 10 patients during the neonatal period. Thirty-eight patients (28.3%) received antiarrhythmic drugs. No atrial fibrillation was observed. Twenty-eight patients (20.9%) presented cardiomyopathy, 9 with supraventricular tachycardia. No association was found between supraventricular tachycardia and another variable. Forty-three patients (32.1%) underwent radiofrequency ablation. A patient suffered sudden death and another patient died during the postoperative period of cardiomyopathy surgery.

Conclusions

1. More than 60% of patients remained asymptomatic. 2) No atrial fibrillation was recorded. 3) Sudden death rate was 0.75%. 4) Patients with supraventricular tachycardia not submitted to ablation had a favorable outcome. 5) Supraventricular tachycardia was not associated with any variable. 6) Multiple conduction pathways always developed supraventricular tachycardia.

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Key words

> Wolff-Parkinson-White syndrome - Pediatrics - Tachyarrhythmias - Congenital cardiomyopathies - Sudden death - Arrhythmia - Catheter ablation

Abbreviations

> AF	Atrial fibrillation	IAC	Interatrial communication
AVNRT	Atrioventricular nodal reentrant tachycardia	PSVT	Paroxysmal supraventricular tachycardia
AV	Atrioventricular	RFA	Radiofrequency ablation
CC	Congenital cardiomyopathies	SD	Sudden death
ECG	Electrocardiogram	VF	Ventricular fibrillation
EPS	Electrophysiology study	WPW	Ventricular pre-excitation or Wolff-Parkinson-White pattern
ERP	Effective refractory period		

INTRODUCTION

Background

The presence of an anomalous muscle bundle or accessory pathway known as the bundle of Kent connects the atria and ventricles independently of the conduction system. (1-4) This allows antegrade ventricular activation from an atrial pulse generating the ventricular pre-excitation or Wolff-Parkinson-White (WPW) pattern in the electrocardiogram (ECG), which is characterized by short PR interval, delta wave and widened QRS. (5)

These bundles also show retrograde conduction with atrial activation from a ventricular stimulus forming a circuit with the conduction system which allows the development of atrioventricular nodal reentrant tachycardia (AVNRT). (6)

The presence of ventricular preexcitation associated with paroxysmal supraventricular tachycardia (PSVT) is called WPW syndrome. (7)

A greater rate of sudden death (SD) than that of the general population has been found in patients affected with WPW. The main mechanism associated with SD would be atrial fibrillation (AF) that spreads to the ventricles due to the WPW, triggering ventricular fibrillation (VF). (8)

Accordingly, the detection of WPW in the pediatric population is considered a SD risk factor, leading to daily life limitations and indication of radiofrequency ablation (RFA) of the WPW, even in asymptomatic patients.

Controversy exists regarding the natural outcome, incidence of arrhythmias and mortality of WPW, which vary according to the population characteristics and age group.

Study Population

The Pediatric Cardiology Unit of the Hospital Nacional "Professor Alejandro Posadas" receives pediatric patients of the Greater Buenos Aires, the Autonomous City of Buenos Aires and the Provinces.

Patients are registered in a database and monitoring is documented in the medical records.

The compilation of history, symptoms, physical examination and complementary studies performed during the initial evaluation and follow-up provide characteristics of patients with WPW.

The present study was undertaken with the purpose of: 1) evaluating the natural history of WPW in a pediatric population, 2) analyzing the presence of PSVT, AF, congenital cardiomyopathies (CC) and the association among PSVT, CC and mortality, and 3) assessing medical treatment.

METHODS

A retrospective, descriptive, observational study of pediatric patients with WPW attending the Pediatric Cardiology clinic at Hospital Nacional "Professor Alejandro Posadas" was performed from March 1976 to March 2011. Inclusion criterion was every patient with ECG compatible with WPW. The Fitzpatrick algorithm was used to determine the WPW anatomical position.

An echocardiogram was performed on all patients to diagnose CC. One hundred and one patients underwent at least a Holter monitoring (75.3%) and an ergometry was performed in 69 patients (51.5%).

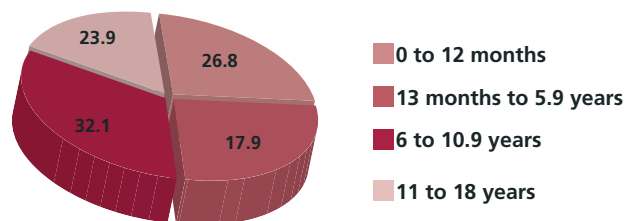
Patients selected to have an electrophysiology study (EPS) and RFA were referred to the Electrophysiology and Pacemaker Section of the Hospital where these procedures were performed.

Data were expressed as mean and standard deviation. Statistical analysis was done using estimated odds ratio, probability and Student's t test. A p value < 0.05 was considered statistically significant.

RESULTS

Among the 134 children included in the study, 80 were boys (59.7%) and 54 were girls (40.3%) (Table 1). Age at WPW diagnosis varied between 2 days and 18 years with a mean value of 6.5 ± 5 years. Age distribution at the moment of diagnosis (Figure 1) was: 0 to 12 months in 36 patients (26.8%), 13 months to 5.9 years in 24 patients (17.9%), 6 to 10.9 years in 43 patients (32.1%) and 11 to 18 years in 32 patients (23.9%).

Fig 1. Percentage of patients with WPW according to age group.



Clinical follow-up was from 1 month to 20 years, with a mean value of 3.6 ± 3.9 years. Four patients had only one consultation.

Reasons for consultation were PSVT in 35 patients (26.1%) and referral for WPW in 16 patients (11.9%). The remaining 83 patients (61.9%) consulted for causes not related to WPW, such as murmur, preschool, pre-sport or pre-surgical assessment, palpitations and suspected CC.

Wolff-Parkinson-White site was left-sided in 76 patients (56.7%), right-sided in 55 patients (41%) and 3 patients (2.3%) had double accessory pathway. Right bundles corresponded to the anterior pathways in 19 patients (14.1%), medioseptal in 13 (9.7%), posterior in 13 (9.7%) and lateral in 10 (7.5%). Left bundles were anterior in 21 patients (15.7%), medioseptal in 7 (5.2%), posterior in 17 (12.7%) and lateral in 31 (23.1%). A family history of WPW was found in 2 patients.

In 16 patients (11.9%) PSVT was registered during follow-up.

Overall, 51 patients (38%) presented with PSVT that corresponded to 17 right pathways (anterior in

Table 1. Demographic characteristic of pediatric patients with WPW

	134	83	51
Population			
Gender, n (%)			
Male	80 (59.7)	50 (60.3)	30 (58.8)
Female	54 (40.3)	33 (39.7)	21 (41.1)
Age at diagnosis			
Mean, years	6.5 ± 5	6.5 ± 4.7	6.3 ± 5.8
Range, days-years	2 d-18 y	10 d-16.7 y	2 d - 18 y
Follow-up			
Mean, years	3.6 ± 3.9	3,3 ± 3,3	4.2 ± 4.6
Range, months-years	1 m-20 y	0 m-15 y	0 m-20 y
Reason for consultation, n (%)			
WPW	16 (11.9)	13 (15.7)	3 (5.9)
PSVT	35 (26.1)	0	35 (68.6)
Others	83 (61.9)	70 (84.3)	13 (25.5)
WPW location, n (%)			
Right	55 (41)	38 (45.8)	17 (33.3)
Anterior	19 (14.1)	15 (18.1)	4 (7.8)
Medioseptal	13 (9.7)	8 (9.6)	5 (9.8)
Posterior	13 (9.7)	9 (10.8)	4 (7.8)
Lateral	10 (7.5)	6 (7.2)	4 (7.8)
Left	76 (56.7)	45 (54.2)	31 (60.8)
Anterior	21 (15.7)	13 (15.7)	8 (15.7)
Medioseptal	7 (5.2)	4 (4.8)	3 (5.9)
Posterior	17 (12.7)	9 (10.8)	8 (15.7)
Lateral	31 (23.1)	19 (22.8)	12 (23.5)
Double	3 (2.2)	0	3 (5.9)
Congenital cardiomyopathies, (n, %)	28 (20.9)	19	9 (32.1)
Pharmacological treatment	38 (28.3)	0	38 (74.5)
EPS and RFA, n (%)	43 (32.1)	15 (18)	28 (54.9)
Right pathways	19 (44.2)	9 (60)	10 (35.7)
Left pathways	21 (48.8)	6 (40)	15 (53.6)
Double pathways	3 (6.9)	0	3 (10.7)
Mortality			
Resuscitated sudden death	1		
Postoperative cardiomyopathy	1		

WPW: Wolff-Parkinson-White pattern. PSVT: Paroxysmal supraventricular tachycardia. EPS: Electrophysiology study. RFA: Radiofrequency ablation.

4 patients, medioseptal in 5, posterior in 4 and lateral in 4), to 31 left pathways (anterior in 8 patients, medioseptal in 3, posterior in 8 and lateral in 12) and to 3 double pathways. In all cases, PSVT was orthodromic.

Age for PSVT emergence was 6.3 ± 5.8 years. In 10 patients PSVT occurred during the neonatal period. No AF was observed.

Age, gender and site of the accessory pathway were analyzed without showing association with PSVT emergence (Table 1). The 3 patients with double pathway had PSVT.

Congenital cardiomyopathy was diagnosed in 28 patients (20.9%) owing to Ebstein's disease in 5 patients, ostium secundum interatrial communication (IAC) in 4, interventricular communication in 3, mitral regurgitation in 2, atrioventricular-ventriculoarterial discordance in 2, bicuspid aorta in 2, dilated car-

diomyopathy in 2, ductus in 1, subaortic membrane in 1, hypertrophic cardiomyopathy in 1, aortic regurgitation in 1, coronary anomaly in 1, atrioventricular-ventriculoarterial discordance + venous sinus type IAC + left superior vena cava + ductus in 1, Ebstein's disease + coarctation of the aorta + IAC in 1 and single left ventricle in 1 patient.

Nine patients with CC suffered from PSVT, but its generation was not associated with presence of CC ($p=0.079$ (Table 2).

One patient presented SD with successful cardiopulmonary resuscitation as first manifestation. One patient died during the immediate postoperative period after total right ventricular bypass surgery, due to low cardiac output.

Pharmacological treatment was prescribed in 38 patients (28.3%) and 11 patients received more than

Table 2. Variable association with paroxysmal supraventricular tachycardia

Abdomen	Confidence interval	p value	Odds ratio	Probability
Male gender	-0.17 a 0.14	0.079	0.94	48.6%
Left pathways	-0.06 a 0.24	0.08	1.53	60%
CC	-0.21 a 0.09	0.079	0.72	41.8%

CC: Congenital cardiomyopathies.

one antiarrhythmic drug. Beta-blockers were used in 27 patients, in 19 of them as single drug, amiodarone in 16 patients, in 8 as single medication, digoxin in 4 patients and flecainide in 1 patient.

Forty-three patients (32.1%) were submitted to EPS and RFA of the accessory pathway (19 right and 21 left pathways), in 8 of the patients due to symptoms compatible with not-registered PSVT and in the remaining 7 due to sports requirement. Three patients presented 2 accessory pathways, one with Ebstein's anomaly and the other two with no evidence of CC. Procedure was successful in 95.3% of cases, with no complications. Radiofrequency ablation was not applied in 5 patients because they presented para-Hisian accessory pathways.

DISCUSSION

During sinus rhythm, ventricular depolarization occurs both through the conduction system and the accessory pathway. (9) The magnitude of the WPW in the ECG depends on the competition between the velocity of conduction and refractoriness of the AV node and the accessory pathway. Both properties are modified during the different stages of childhood. (10) Wolff-Parkinson-White prevalence ranges from 0.1 to 0.3% in the general population; (28) and each year 4 new cases are produced every 100000 subjects. (11)

Males have been reported to be more affected than females, (12) in a 2:1 proportion. We did not find that predominance in our population.

The highest detection of new cases is found during the first year of life in both genders, 20/100000 males and 6/100000 females, (13) a characteristic which was preserved in our population.

Paroxysmal supraventricular tachycardia

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most frequent cause of PSVT during childhood, varying from 60% (14) to 70% (15) of cases. It can be orthodromic or antidromic. In orthodromic AVNRT, antegrade conduction courses along the conduction system and atrial retrograde activation occurs through the WPW. (16) In 5% to 10% of patients with WPW AVNRT is antidromic, with inverted circuit. (17) In the study population, all cases of PSVT were of orthodromic AVNRT origin and no variable was associated with the emergence of AVNRT. All patients with double pattern WPW experienced tachycardia.

Congenital cardiomyopathies

Wolff-Parkinson-White is more frequent in patients

with CC, with a prevalence of 2.7 to 8.6/1000 cases. (18)

Ebstein's disease is the most commonly associated CC (10-30%), as well as various types of single ventricle, atrioventricular-ventriculoarterial discordance and interatrial septum defects, tricuspid valve anomalies and ventricular defects, (12) an association that is preserved in our casuistic records.

Multiple accessory pathways have been found in 50% of patients with Ebstein's disease, (18) with predominance of right-sided pathways.

Patients with CC undergoing Mustard, Senning, Ebstein and Fontan-Kreutzer surgeries are at risk of presenting with tachycardia, flutter and AF in addition to the WPW. (18).

Mortality

Rate of WPW mortality is very different according to the series analyzed.

Follow-up studies and natural outcome of young adults with WPW, most of them asymptomatic, suggest a very low rate of SD. Among these studies, it is worth mentioning the series of Fitzsimmons et al. (19) of 228 males during 22 years, with a death rate of 0.02%/year, that of Munger et al. (13) with 113 patients during 35 years, with SD incidence of 0.0015% (CI 0.002-0.005), without episodes of SD in asymptomatic patients, and that of Brembilla et al. (20) with 195 patients during 20 years, with a SD rate of 0.002%. The weakness of these series is the number of patients lost to follow-up.

In 124 asymptomatic pediatric patients with follow-up of 4.2 years (21) and Holter monitoring every year, no health problems were detected and no AF was registered. In this series, 3.4% of patients presented PSVT.

In the series mentioned above, no EPS were performed in asymptomatic patients. Pappone et al. carried out EPS in symptomatic children with WPW; he induced PSVT in 27.7% of them and in 10% asymptomatic patients > 18 years (22, 23) and found a higher incidence of severe arrhythmic complications. (11) They concluded that mortality was 10 times higher, with a rate of 0.5%/year. (22, 24-26)

Coincident with reported findings, Kantoch (12) describes very low risk of SD or heart failure in children and adolescents with PSVT, except in: 1) neonatal patients with PSVT, 2) WPW and 3) children with CC. Normally, pediatric patients exhibit faster conduction than adults. (27)

Fast PSVT can be the only cause or facilitate the

emergence of SD due to cardiovascular collapse or association with CC, produce secondary dilated cardiomyopathy, coronary ischemia and degeneration to VF. (28) None of these complications were detected in our series.

The mechanism of arrhythmic SD in the WPW syndrome is pre-excitation AF or atrial flutter with extremely fast AV conduction through the WPW as bystander or passage, (17) and subsequent deterioration to ventricular flutter or VF. (8)

In the series of asymptomatic pediatric patients with WPW reported by Sarubbi et al., (29) AF was registered in 1/57 patients. During follow-up of 184 children, Pappone et al. (22) induced AF in those presenting the shortest antegrade effective refractory period (ERP) of the accessory pathway, multiple pathways and retrograde conduction of the WPW (12% of patients). We have not documented AF in our patients, either spontaneously or in EPS.

Harahsheh et al. (30) studied the spontaneous degeneration of PSVT to AF/flutter in children with WPW. In 50% of patients, AF was induced and 67% of them presented fast ventricular response. The only risk factor was the right-sided location of the WPW.

According to Pappone et al., (24) EPS and induction of sustained AF in asymptomatic children with WPW are the important risk markers of SD, attributing less importance to antegrade ERP of the accessory pathway. The non-induction of AF in childhood does not mean that it cannot be developed later. (31)

It has been suggested that in asymptomatic WPW the childhood pathways disappear during the passage into adult life, decreasing risk. (23) However, the increased prevalence of AF with age is not taken into account. (11) In almost half of the patients resuscitated from episodes of SD this was the first symptomatic arrhythmia they had experienced. (32)

Dubin et al. (33) compared the electrophysiologic findings of symptomatic children with the electrocardiographic manifestations of asymptomatic children with WPW. None of the variables presented differences, which suggests that SD risk factors developed for adults are not clearly applicable in children.

Our study reported a case of SD receiving cardiopulmonary resuscitation maneuvers but without studies to rule out myocardial pathology triggering VT/VF. The weakness of our results lies in the characteristics of the retrospective analysis.

To our knowledge, there are no series of patients with WPW and SD episodes who have had an anatomopathological study to exclude sub-diagnosed pathologies associated with the WPW or confirm the influence of the accessory pathway in the final mechanism of SD.

Medical treatment

Evaluation and follow-up of patients with WPW has gradually changed. Zipes et al. (34) suggest a non-invasive evaluation with ECG, ergometry, echocardiogram and Holter monitoring, diagnostic methods

generally used in our population.

The invasive strategy and empirical RFA in asymptomatic children is controversial, but is progressively increasing. (35) Classical measurements of EPS are antegrade ERP of the pathway, shorter RR interval during atrial stimulation, multiple pathways and bundle localization, (18) and induced AF with RR interval < 250 ms. (22, 25) The present study has not analyzed the characteristics found in invasive procedures, which could be subject for a future study.

In 165 children, Pappone et al. established that independent predictors of arrhythmic events are absence of prophylactic ablation and presence of multiple pathways. Wellens et al. (11) point out that to discover 165 ECG of children with WPW required 200000 ECGs, which is an unusual practice in many countries. In our Service, an ECG is systematically performed at the first evaluation of all patients.

Radiofrequency ablation is the treatment of choice for pediatric patients with symptomatic tachyarrhythmias (22, 35-37)

The experience of the center is extremely important. (31)

In a comparative study of RFA between children and adults (15) and another of 231 children with RFA for PSVT (14) no significant differences were found between procedure duration and time of fluoroscopy, with 92% success rate, 12.5% recurrence and 2% major complications. Our population did not present complications with a similar success rate.

In children, free wall and anteroseptal right pathways were more frequent. (15) No predominant location was found in our population.

CONCLUSION

Different series results have modified management of asymptomatic children with WPW.

The first works showed low incidence of SD, a benign approach in the absence of symptoms and attempts to stratify SD risk with non-invasive methods. Progressively, it was seen that they were not enough to detect cases of life-threatening tachyarrhythmias. In our population, more than 60% of patients with WPW remained asymptomatic until adulthood.

The last decade posed the need of performing EPS in asymptomatic patients to stratify risk in a more precise manner.

Risk factors are induction of AF, antegrade ERP of the pathway or RR cycle < 250 ms during AF and the association with multiple pathways and CC, and more questionably, age. In our series there were no variables associated with PSVT. Patients with double pathways presented PSVT. No AF was reported. The rate of SD was 0.75%, despite most of our patients presented some risk factor.

Radiofrequency ablation is the treatment of choice for symptomatic children or those presenting SD risk factors. In the study population, patients with PSVT not undergoing ablation had a good outcome.

RESUMEN

Seguimiento de 134 pacientes pediátricos con patrón de Wolff-Parkinson-White: evolución natural e intervención médica***Objetivos**

Analizar los factores de riesgo vascular en mujeres climatéricas. Investigar las diferencias de estos factores entre las premenopáusicas y las posmenopáusicas. Evaluar la presencia de hipertensión arterial, diabetes mellitus y/o dislipidemia en asociación con la edad y/o la posmenopausia.

Material y métodos

Estudio descriptivo observacional. Se registraron pacientes con preexcitación ventricular en el electrocardiograma desde 1976 a 2011. Todos tenían ecocardiograma, 101 pacientes Holter (75,3%) y 69 (51,5%) ergometría. En pacientes seleccionados se realizó ablación por radiofrecuencia. Los datos se expresaron como media y desviación estándar.

Resultados

Se incluyeron en el estudio 134 pacientes, 80 varones (59,7%). Edad al diagnóstico: 2 días a 18 años, media $6,5 \pm 5$ años. Seguimiento clínico: 1 mes a 20 años, media $3,6 \pm 3,9$ años. Consultaron por taquicardia supraventricular 35 pacientes (26,1%), por preexcitación ventricular 16 pacientes (11,9%) y por otras causas 83 pacientes (61,9%); 76 pacientes (56,7%) evidenciaron vía izquierda, 3 pacientes doble vía; 16 pacientes (11,9%) presentaron taquicardia supraventricular durante el seguimiento. En total, 51 pacientes (38%) tuvieron taquicardia ortodrómica a los $6,3 \pm 5,8$ años, 10 pacientes en el período neonatal; 38 pacientes (28,3%) recibieron antiarrítmicos. No se observó fibrilación auricular. Veintiocho pacientes (20,9%) presentaron cardiopatía, 9 con taquicardia supraventricular. No hubo variables vinculadas con taquicardia supraventricular. En 43 pacientes (32,1%) se realizó ablación por radiofrecuencia. Un paciente murió súbitamente. Otro paciente falleció en el posoperatorio de cardiopatía.

Conclusiones

1) Más del 60% de los pacientes permanecieron asintomáticos. 2) No se registró fibrilación auricular. 3) La tasa de muerte súbita fue del 0,75%. 4) Los pacientes con taquicardia supraventricular no sometidos a ablación evolucionaron bien. 5) No se asociaron variables con taquicardia supraventricular. 6) Las vías múltiples siempre desarrollaron taquicardia supraventricular.

Palabras clave > Síndrome de Wolff-Parkinson-White - Pediatría - Taquiarritmias - Cardiopatías congénitas - Muerte súbita - Arritmia - Ablación con catéter

Conflicts of interest

None declared.

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