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Original Article

Use of electrophysiologic testing to assess risk in children with Wolff-Parkinson-White syndrome

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Abstract In adults with Wolff-Parkinson-White syndrome, the likelihood of sudden death can be estimated based upon the presence or absence of symptoms. Comparable data in children do not exist. To date, therefore, invasive risk stratification has been used to guide management regarding radiofrequency ablation in symptomatic children. As the safety of electrophysiology study and radiofrequency ablation in children has improved, asymptomatic patients have been referred more commonly for invasive risk stratification. We sought to compare the findings from electrophysiologic studies in symptomatic children with Wolff-Parkinson-White syndrome to the findings in asymptomatic children with Wolff-Parkinson-White pattern on their electrocardiogram. Thus, we compared the findings from electrophysiologic studies carried out in patients seen at Stanford University and University of California, San Francisco, from April 1999 to February 2001 with a preexcitation pattern on their electrocardiogram. The patients were divided into three groups: 23 asymptomatic patients studied for risk stratification, 19 patients who presented with syncope, and 77 patients presenting with documented supraventricular tachycardia. Data were collected for commonly accepted invasive criterions for stratification of risk: an effective refractory period of the accessory pathway less than 270 ms, multiple pathways, septal location of pathway, and inducibility of supraventricular tachycardia. Groups were compared by chi-square. No differences were found between the groups for any of the variables. These data suggest that risk factors for sudden death, developed in studies of adult patients, are not clearly applicable to children. Further studies are needed better to define the indications for study and ablation in children.

Keywords: Childhood; Wolff-Parkinson-White; stratification of risk; invasive studies

In adults with Wolff-Parkinson-White syndrome, there is a well-established relationship between the presence of symptoms and the risk of sudden death. Natural history studies of asymptomatic patients with Wolff-Parkinson-White syndrome have shown a rate of sudden death of 1 per 1000 patient years of follow-up,[1] whereas in a study of comparable symptomatic patients, ventricular fibrillation occurred in 2.2% of patients over a 16 year period.[2] Retrospective studies of invasively determined conduction characteristics of accessory pathways have supported the use of electrophysiologic studies for the identification of adults who might be at risk of ventricular fibrillation. These proposed characteristics have included: an effective refractory period of less than 270 ms for antegrade conduction across the accessory pathway, the presence of septal accessory pathways, and the presence of multiple pathways.[2–4] While there is general agreement concerning the need for some type of stratification of risk in symptomatic adults, the role of such testing in asymptomatic individuals is controversial.

In contrast to adults, risk assessment for children is less well supported by clinical research, and represents a considerable clinical challenge. The incidence of sudden death in children with Wolff-Parkinson-White

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syndrome is not defined. While sudden death is rare in childhood, it may be related to Wolff-Parkinson-White syndrome more commonly than is generally appreciated. In fact, Silka and colleagues[5] have described a cohort of children surviving an episode of "near-miss" sudden death in which one-fifth had Wolff-Parkinson-White syndrome.

The lifetime incidence of sudden death in a symptomatic child with Wolff-Parkinson-White syndrome has been estimated at 3–4%.[6–8] This, too, may be an underestimate since the natural history studies draw heavily from adult cohorts, who have by definition survived to adulthood, and may therefore be at lower risk. Furthermore, there may be little or no warning prior to a catastrophic event in the child with Wolff-Parkinson-White syndrome. Almost half of children suffering cardiac arrest with Wolff-Parkinson-White syndrome had no prior important clinical events.[9]

While invasive electrophysiologic evaluation is often used for estimation of risk prospectively in symptomatic children, clinical studies have not been performed in children with few or no symptoms. Asymptomatic children, nonetheless, are increasingly being referred for invasive electrophysiologic evaluation. Clearly, both the importance of presence or absence of symptoms, and the role of electrophysiologic evaluation in stratification of risk, need to be evaluated in children. We report here a study of consecutive children with Wolff-Parkinson-White syndrome with and without cardiac symptoms who underwent invasive electrophysiologic testing. We reasoned that, if the presence of cardiac symptoms is an important risk factor in such children, then invasively determined electrophysiologic characteristics should be different in symptomatic and asymptomatic patients.

Methods

Study

We included in the study consecutive children with preexcitation on their electrocardiogram, with and without a history of tachycardia or other cardiac symptoms, who underwent electrophysiologic testing from April 1999 to February 2001 at the Pediatric Arrhythmia Center at University of California, San Francisco and Stanford. Electrophysiologic studies were performed under general anaesthesia for those children less than 13 years old, and with conscious sedation for those 13 years old or greater. The refractory period of the accessory pathway was determined by pacing the high right atrium at a cycle length of 400 ms. The determination of refractory period was repeated by pacing from the middle pair of a decapolar electrode catheter placed in the coronary sinus. The effective refractory period was recorded as the longest A1/A2 interval that consistently failed to conduct in the accessory pathway, measured at the site closest to the pathway.

Isoproterenol was employed when tachycardia was not inducible in the baseline state. Atrial fibrillation was not routinely induced.

Risk factors

The presence or absence of each of the following reported or proposed risk factors was noted:

- Effective refractory period of the accessory pathway less than 270 ms.
- Multiple accessory pathways.
- Septal accessory pathway.
- Inducibility of orthodromic atrioventricular reciprocating tachycardia.
- Inducibility of antidromic atrioventricular reciprocating tachycardia.

Groups of patients

Patients were grouped according to symptoms that were present prior to the study, as follows:

- Asymptomatic patients studied for stratification of risk.
- Patients with history of syncope.
- Patients with documented supraventricular tachycardia or palpitations.

Analysis

Continuous data were compared using analysis of variance, and frequency data were analyzed using the chi-square test.

Results

General

We carried out 123 electrophysiologic studies in 119 patients with pre-excitation on their electrocardiogram between April 1999 and February 2001. Of the children, 65 (55%) were male. Structural heart disease was found in 4 children, mild Ebstein's malformation in 2, valvar pulmonary stenosis in 1, and repaired ventricular septal defect in the other.

We included 23 asymptomatic patients, 19 with syncope; and 77 with supraventricular tachycardia or palpitations. The groups were similar with respect to demographic factors (Table 1). None of the children in any group had presented with aborted sudden death.

Risk factors

Table 2 lists the number of patients in each group with previously reported or proposed risk factors,

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as defined in Methods. No significant differences between groups were observed with respect to presence or absence of risk factors, by chi-square analysis. None of the proposed risk factors, therefore, distinguished between symptomatic and asymptomatic children. Atrioventricular nodal reentrant tachycardia could be elicited in 5% of each group (5%). No difference could be identified for the location of the pathways in any of the three groups, and each group had a similar incidence of septal pathways. The measured effective refractory periods of the pathways were shown, by analysis of variance, to be similar in all three groups (Fig. 1). The measured effective refractory periods were not any shorter in patients with symptoms, even symptoms of syncope, than in completely asymptomatic patients. Of note, orthodromic atrioventricular reentrant tachycardia was inducible in 61% of previously asymptomatic patients, 2 of 23 had effective antegrade refractory periods of the than 240 ms, and 2 of 23 had inducible antidromic atrioventricular reentrant tachycardia.

Ablation

Radiofrequency ablation was attempted more frequently in the syncopal patients, and those with supraventricular tachycardia, than in those who were asymptomatic, as would be expected from the indications for referral (Table 3). The procedure was attempted in 19 of the 23 asymptomatic children, in all the children suffering syncope, and in 75 of the 78 with supraventricular tachycardia ($p = 0.01$). Recurrences occurred in one of the asymptomatic patients, none of those presenting with syncope, and 2 of those with supraventricular tachycardia.

Isoproterenol

Isoproterenol, at 025 mcg/kg/minute, was administered to 31 patients; 12 of the asymptomatic children, 5 of the children presenting with syncope, and 14 of those with supraventricular tachycardia. There was a significant decrease in the effective refractory period of the accessory pathway in each group with the addition of isoproterenol (Fig. 2). There was a significantly larger decrease in this effective refractory period in those who were syncopal when compared to the asymptomatic children or those with supraventricular tachycardia (147 ± 135 ms versus 78.5 ± 62.8 ms and 45.4 ± 34.9 ms, respectively,

Table 1. Demographics of the groups of patients.

	Asymptomatic patients	Syncopal patients	Patients with supraventricular tachycardia and/or palpitations	p
Patients	23	19	77	
Age (range)	11.8 ± 4.3 (3.8–17.8)	14.3 ± 3.8 (5.0–18.5)	13.3 ± 3.9 (4.0–21.2)	NS*
Sex (M%)	14 (61%)	9 (47%)	42 (55%)	NS†
CHD	3	0	1	NS†

*By analysis of variance, †by chi-square.
Abbreviaitons: M: male; CHD: congenital heart disease

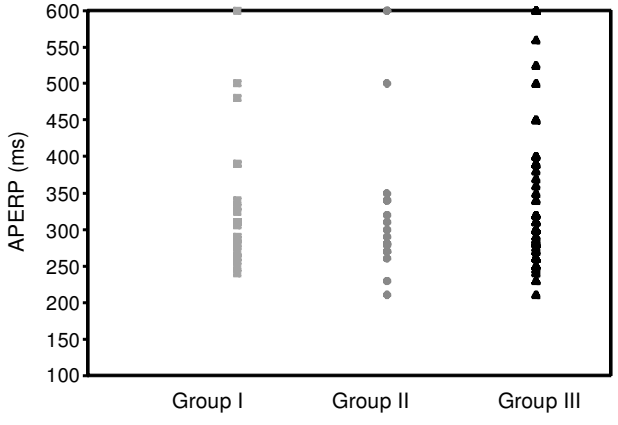

Figure 1.
Range of effective refractory periods of the accessory pathways in milliseconds according to group. APERP: effective refractory period of the accessory pathway.

Table 2. Invasive criterions for risk by group.

	Asymptomatic patients	Syncopal patients	Patients with supraventricular tachycardia and/or palpitations	p*
APERP ⩽ 240 ms	2/23 (9%)	3/19 (26%)	9/77 (12%)	NS
APERP ⩽ 270 ms	8/23 (35%)	8/19 (42%)	22/77 (29%)	NS
Multiple AP	5/23 (22%)	0/19 (0%)	5/77 (6%)	NS
Septal AP	10/23 (43%)	8/19 (42%)	26/77 (34%)	NS
Inducible SVT	14/23 (61%)	14/19 (74%)	56/77 (73%)	NS
Antidromic SVT	2/23 (9%)	2/19 (11%)	1/77 (1%)	NS
AVNRT	2/23 (8%)	1/19 (5%)	3/77 (4%)	NS

*By chi-square.
Abbreviations: APERP: effective refractory period of the accessory pathway; AP: accessory pathway; SVT: supraventricular tachycardia; AVNRT: atrioventricular nodal reentrant tachycardia

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Table 3. Radiofrequency ablation by group.

	Asymptomatic patients	Syncopal patients	Supraventricular tachycardia/palpitations	p*
Attempted ablation	19/23 (83%)	19/19 (100%)	75/78 (96%)	0.01
No WPW when last seen	18/19 (95%)	19/19 (100%)	73/75 (94%)	NS
Complications	0/23 (0%)	0/19 (0%)	0/75 (0%)	NS

*By chi-square.
Abbreviations: RF: radiofrequency; WPW: Wolff-Parkinson-White syndrome

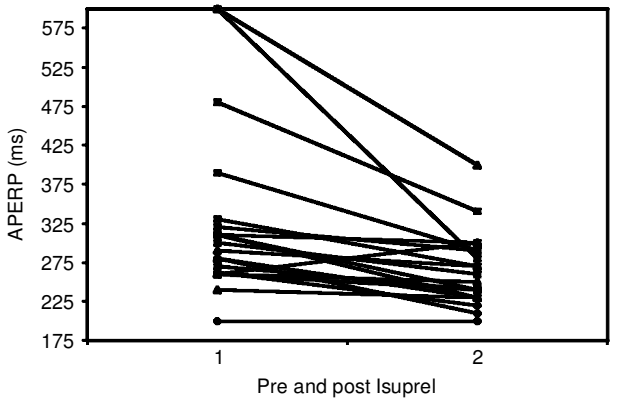

Figure 2.
Change in the effective refractory period in milliseconds with addition of isoproterenol. APERP: effective refractory period of the accessory pathway.

mean ± standard deviation, $p = 0.02$, analysis of variance).

Discussion

Much has been written about the risk of sudden death, and the stratification of risk, in adults with Wolf-Parkinson-White syndrome, but no comparable studies have been reported in children.[2–4,10–16] Our study shows that commonly accepted invasive criterions for risk criteria in adults do not differentiate asymptomatic from symptomatic children with Wolff-Parkinson-White syndrome. There are two possible explanations for this observation. First, it may be that standard risk factors for adults, such as the effective refractory period of the accessory pathway, are invalid when applied to children. Timmermans and colleagues[2] have shown that a septal location of the accessory pathway is related to risk of sudden death in adults. This has never been corroborated in children. Russell and colleagues[17] found that, in their series of 256 children, those who presented with cardiac arrest all had left-sided pathways. Similar results were found by Bromberg et al.,[18] who studied symptomatic children presenting for surgical ablation. In our population, in contrast, there was no relationship between location or number of pathways, the effective refractory period of the pathway, a history of syncope, sudden death, or supraventricular tachycardia.

A second, alternative, explanation for our findings is that the group of "asymptomatic" children includes a large number who are destined to develop symptoms by adulthood, diluting potential differences between groups. Indeed, more than half of our asymptomatic patients were found to have inducible atrioventricular reentrant tachycardia at the time of the electrophysiologic study, and 2 of 23 had antidromic atrioventricular reentrant tachycardia. Clinical history plays a large role in the management of adults with Wolff-Parkinson-White syndrome. Syncope, and atrial fibrillation with rapid ventricular rates, are commonly regarded as warning arrhythmias. In children, our data suggest that the lack of such clinical characteristics might not necessarily be reassuring. Deal and colleagues,[9] in their multicentric study, found that no prior arrhythmia had been documented in almost half of children who had Wolff-Parkinson-White syndrome and who suffered a cardiac arrest. This finding was confirmed by Bromberg and colleagues.[18] They found no warning signs in 9 of their 10 patients who experienced clinical cardiac arrest. Our findings are consistent with these data, as our patients with syncope have, on average, the same electrophysiologic "profile" as those who are asymptomatic. This may reflect the fact that asymptomatic children may simply not have lived long enough to develop symptoms.

Studies in the adult population have shown that isoproterenol will shorten the refractory periods from a baseline state.[19,20] No data exist, however, which suggest that isoproterenol can be used as a prognostic predictor. Isoproterenol appears to have shortened the effective refractory period of the accessory pathway in the syncopal patients more than in those with supraventricular tachycardia or those who were asymptomatic. The numbers studied were small, and further work is needed to look more closely at the relationship between the behaviour of the accessory pathway when challenged by isoproterenol and clinical symptoms.

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There are several further limitations to our study. Sudden death and ventricular fibrillation are rare events in children, and are infrequently observed in children with Wolff-Parkinson-White syndrome.[21] Despite the fact that our series represents consecutive patients referred for electrophysiologic study over nearly 2 years, it includes no patients who initially presented with aborted sudden death and/or ventricular fibrillation. We do not routinely induce atrial fibrillation in our patients and we did not use isoproterenol in all of them. We also have not commented on non-invasive means of assessing risk, as we were striving to try and assess the use of invasive criterions for risk in this population.

Electrophysiologic studies, and radiofrequency ablation, have become quite safe in children.[22] Perhaps as a result of this fact, asymptomatic children are increasingly being referred for electrophysiologic evaluation, with ablation when appropriate. At the same time, the number of adults undergoing ablation has decreased markedly.[23] Increasingly, Wolff-Parkinson-White syndrome is becoming a disease of childhood. Risk factors for sudden death, developed in studies of adults, are not clearly applicable to children. Further studies are needed better to define the indications for study and ablation in childhood.

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