ELECTROPHYSIOLOGY

Intermittent versus Persistent Wolff-Parkinson-White Syndrome in Children: Electrophysiologic Properties and Clinical Outcomes

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Background: *Intermittent Wolff-Parkinson-White (WPW) syndrome is considered to have a lower risk of sudden death. Fewer data exist regarding electrophysiologic (EP) characteristics and the natural history of intermittent WPW in children.*

Methods: *All patients with WPW age 1–18 years at a single institution (1996–2013) were reviewed. Patients with intermittent preexcitation were compared to those with loss of preexcitation on Holter/exercise testing and those with persistent preexcitation. High-risk accessory pathway (AP) was defined as AP effective refractory period (APERP), block cycle length, or shortest preexcited RR interval during atrial fibrillation ≤250 ms.*

Results: *A total of 295 patients were included: 226 (76.6%) persistent, 39 (13.2%) intermittent, and 30 (10.2%) loss of preexcitation Holter/exercise. There were no differences in symptoms between groups. Median interquartile range APERP was significantly longer in intermittent WPW (380 [320, 488] ms vs 320 [300, 350] ms persistent, 310 [290, 330] ms loss of preexcitation Holter/exercise; P = 0.0008). At baseline, there was no difference between groups in frequency of high-risk pathways. However, when isoproterenol values were included, high-risk pathways were more frequent among patients with loss of preexcitation on Holter/exercise (54% vs 16% persistent, 11% intermittent; P = 0.005). There was one death in a patient with loss of preexcitation on exercise testing, no EP study, and prior drug use. A second patient with persistent WPW and APERP 270 ms required resuscitation following a methadone overdose.*

Conclusion: *Intermittent preexcitation in children does not connote a lower risk AP by EP criteria or reduced symptoms. The low number of pediatric WPW patients who develop preexcited atrial fibrillation or sudden death warrants larger studies to investigate these outcomes. (PACE 2016; 39:14–20)*

ventricular preexcitation, Wolff-Parkinson-White syndrome, intermittent preexcitation, children, risk stratification

Introduction

Intermittent preexcitation in Wolff-Parkinson-White (WPW) syndrome has historically been thought to confer a lower risk of sudden cardiac death than persistent preexcitation.[1] Accessory pathways (APs) in intermittent WPW have been thought to have longer refractory periods and therefore lower risk for development of sustained preexcited atrial fibrillation or ventricular fibrillation.[1] In prior studies of patients with WPW, risk factors for development of these potentially life-threatening arrhythmias have included documented atrial fibrillation,[2] inducible reciprocating tachycardia,[3,4] multiple APs,[2–5] and an AP effective refractory period (APERP) or shortest preexcited RR interval less than 250 ms.[2–5]

However, fewer data exist regarding pediatric patients with intermittent WPW. The 2012 expert consensus statement by the Pediatric and Congenital Electrophysiology Society (PACES) and Heart Rhythm Society (HRS) on treatment of asymptomatic, intermittent WPW recommends against routine invasive electrophysiologic (EP) study (EPS).[6] One prior study has directly compared pediatric patients with persistent versus intermittent WPW and did not find a significant difference in the frequency of high-risk APs between groups, suggesting the intermittent nature of an AP may not rule out potentially high-risk conduction characteristics. However, it should be

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noted in that study, patients with intermittent WPW and who were asymptomatic (n = 5) all had low-risk pathways on invasive electrophysiology study. Based on these findings, the authors supported the PACES/HRS recommendations in asymptomatic patients. Because of small sample sizes and limited data, the optimal management of patients with intermittent WPW by electrocardiogram (ECG) criteria remains unclear. This study details the natural history, clinical presentation, and EP characteristics of pediatric patients with intermittent versus persistent WPW.

Methods

The study protocol was approved by the Institutional Review Board of the University of Colorado.

All patients who presented to Children's Hospital Colorado between 1996 and 2013 and carried a diagnosis of WPW syndrome were retrospectively reviewed. Inclusion criteria were age 1–18 years at presentation, confirmed ventricular preexcitation on at least one surface ECG, and at least two available ECGs for review. Exclusion criteria were ventricular preexcitation or supraventricular tachycardia prior to 1 year of age, hemodynamically significant congenital heart disease, or previous ablation procedure(s) at an outside institution. Patients with minor congenital heart disease (patent foramen ovale, patent ductus arteriosus, small atrial or ventricular septal defect, or mitral valve prolapse) were included.

Patients were categorized into one of three groups: (1) persistent preexcitation, defined as preexcitation present on all preablation surface ECGs and throughout exercise testing and Holter monitoring, if performed; (2) intermittent preexcitation, defined as having no preexcitation or sudden loss of preexcitation on at least one preablation baseline surface ECG; and (3) loss of preexcitation only with increased heart rates on exercise testing or Holter monitoring. Exercise testing was performed to maximum exertion with a modified Bruce protocol on either a bicycle or treadmill. Holter monitoring used a standard three-lead monitor, and all findings were reviewed by a pediatric electrophysiologist. The decision to perform exercise testing or Holter monitoring was at the discretion of the primary cardiologist.

Clinical data collected included baseline demographic information, symptoms present at presentation, symptoms developed on follow-up evaluations, length of follow-up, and clinical outcomes including development of preexcited atrial fibrillation and death.

Electrophysiologic Study

EPSs were performed at the discretion of the attending electrophysiology physician. All EPSs were invasive four-wire studies with standard lead placement in the high right atrium, His bundle, coronary sinus, and right ventricular apex, and were conducted under general anesthesia. No patients underwent an esophageal study. APs were investigated to determine their location, APERP, AP retrograde effective refractory period (APRERP), block cycle length (BCL), and shortest preexcited R-R interval during atrial fibrillation, if induced. Induction of atrial fibrillation was not routine practice. An AP was considered high risk if the APERP, BCL, or shortest preexcited RR interval was ≤250 ms, on or off of isoproterenol. Isoproterenol was administered at physician discretion, starting at 0.05 mcg/kg/hour and titrating up to a heart rate 20% above baseline. Data were also gathered regarding the inducibility of supraventricular tachycardia or preexcited atrial fibrillation, whether an ablation was performed, ablation success, type of ablation performed (radiofrequency vs cryoablation), and any complications of the procedure.

Statistics

Statistical analysis was performed using SAS software version 9.3 (SAS Institute, Cary, NC, USA). Data are reported as medians with interquartile ranges for nonparametric data, means with 95% confidence intervals for normally distributed data, or frequencies with percentages, as indicated. χ^2 or Fisher's exact tests were used for comparisons between groups of binary/categorical data. Analysis of variance or Kruskal-Wallis testing were performed on continuous variables. A P value of ≤0.05 was considered statistically significant.

Results

Demographics and Clinical Data

There were 295 patients who met inclusion criteria for the study: 226 (76.6%) with persistent WPW, 39 (13.2%) with intermittent WPW by baseline ECG, and 30 (10.2%) with loss of preexcitation on exercise testing or Holter monitoring. There were no significant differences in baseline demographics between groups (Table I). The groups also did not differ in their distribution of presenting symptoms or in symptoms developed throughout the course of their follow-up (Table II). These findings did not differ for the subgroup of patients who did not undergo EPS, which may represent our best approximation of the natural history of WPW in children (Table III). For all groups, palpitations were the most common symptom reported. Two patients in the persistent WPW group presented with preexcited atrial fibrillation, and none in any group subsequently developed preexcited atrial fibrillation (P = 1.00).

Table I.

Baseline Demographic and Clinical Data

	Persistent WPW (n = 226)	Intermittent WPW (n = 39)	Loss of WPW on Holter/Exercise (n = 30)	P Value
Male	123 (54%)	23 (59%)	16 (57%)	0.82
Age at presentation (years)	12.0 [11.4, 12.6]	12.2 [10.8, 13.6]	11.4 [9.8, 13.0]	0.74
Minor congenital heart disease	12 (5%)	1 (3%)	4 (13%)	0.15
Exercise stress testing	28 (12%)	8 (21%)	15 (50%)	<0.0001
Holter monitoring	23 (10%)	10 (26%)	20 (67%)	<0.0001
Length of follow-up (months)	260 [69, 729]	508 [69, 993]	288 [83, 675]	0.52

WPW = Wolff-Parkinson White syndrome.

Table II.

Symptoms in the Entire Patient Group

	Persistent WPW (n = 226)	Intermittent WPW (n = 39)	Loss of WPW on Holter/Exercise (n = 30)	P Value
Chest pain	73 (32%)	13 (33%)	7 (23%)	0.66
Palpitations	159 (70%)	27 (69%)	18 (60%)	0.51
Syncope	49 (22%)	5 (13%)	3 (10%)	0.10
Clinical preexcited atrial fibrillation	2 (0.9%)	0 (0%)	0 (0%)	1.00
Sudden arrest	1 (0.4%)	0 (0%)	1 (3%)	0.21
Other	6 (3%)	2 (5%)	2 (7%)	0.24
Asymptomatic	36 (16%)	7 (18%)	7 (23%)	0.59

WPW = Wolff-Parkinson White syndrome.

Table III.

Symptoms in Patients Who Did Not Undergo Electrophysiology Study

	Persistent WPW (n = 20)	Intermittent WPW (n = 12)	Loss of WPW on Holter/Exercise (n = 14)	P Value
Chest pain	0 (0%)	2 (17%)	2 (14%)	0.15
Palpitations	6 (30%)	4 (33%)	55 (36%)	1.00
Syncope	0 (0%)	0 (0%)	0 (0%)	1.00
Clinical preexcited atrial fibrillation	0 (0%)	0 (0%)	0 (0%)	1.00
Sudden arrest	0 (0%)	0 (0%)	1 (7%)	0.57
Other	0 (0%)	0 (0%)	1 (7%)	0.57
Length of follow-up (months)	257 [14, 862]	105 [32, 948]	95 [61, 602]	0.96

Neither patient who presented with preexcited atrial fibrillation progressed to cardiac arrest. One patient died who had loss of preexcitation on exercise testing, no prior EPS, and a known history of prior drug use. Another patient with persistent WPW required resuscitation likely secondary to a methadone overdose. She underwent EP study and ablation following her arrest and was found to have an APERP of 270 ms. In both cases, it was unclear whether WPW contributed to the arrest.

Table IV.

Electrophysiologic Data

	Persistent WPW (n = 226)	Intermittent WPW (n = 39)	Loss of WPW on Holter/Exercise (n = 30)	P Value
Underwent EPS	**206 (91%)**	**26 (68%)**	**16 (53%)**	**<0.0001**
Age at EPS (years)	12.7 [12.1, 13.3]	14.3 [12.6, 15.9]	11.9 [9.8, 14.0]	0.15
Weight at EPS (kg)	53.7 [50.3, 57.0]	59.1 [49.8, 68.5]	44.8 [32.7, 56.9]	0.18
Patients tested on isoproterenol	18 (8%)	3 (8%)	3 (10%)	0.93
APERP (ms)	**320 [300, 350]**	**380 [320, 488]**	**310 [290, 330]**	**0.0008**
AP block cycle length (ms)	**310 [280, 370]**	**410 [320, 500]**	**280 [250, 320]**	**0.0001**
AP block cycle length on isoproterenol (ms)	275 [235, 310]	240 [240, 280]	220 [200, 220]	0.12
Preexcited atrial fibrillation during EPS	13 (6%)	0 (0%)	0 (0%)	0.20
High-risk AP (baseline)	*21* (*12%*)	*1* (*5%*)	*4* (*31%*)	*0.09*
by APERP	*4* (*2%*)	*1* (*5%*)	*0* (*0%*)	
by BCL	*19* (*11%*)	*0* (*0%*)	*4* (*31%*)	
by RR interval in AF	*2* (*1%*)	*0* (*0%*)	*0* (*0%*)	
High-risk AP (baseline or isoproterenol)	*28* (*16%*)	*2* (*11%*)	*7* (*54%*)	*0.005*
by APERP	*8* (*4%*)	*2* (*11%*)	*2* (*15%*)	
by BCL	*26* (*14%*)	*2* (*11%*)	*7* (*54%*)	
by RR interval in AF	*2* (*1%*)	*0* (*0%*)	*0* (*0%*)	
Inducible reciprocating tachycardia	99 (50%)	10 (42%)	9 (56%)	0.63
Retrograde conduction	134 (72%)	18 (78%)	14 (93%)	0.19
Pathway location				0.15
Left free wall	79 (44%)	15 (71%)	6 (43%)	
Right free wall	46 (25%)	2 (10%)	5 (36%)	
Septal	57 (31%)	4 (19%)	2 (21%)	
Ablation performed	177 (86%)	19 (73%)	14 (88%)	0.23

Boldface denotes significant findings. AF = atrial fibrillation; AP = accessory pathway; APERP = AP effective refractory period; BCL = block cycle length; EPS = electrophysiologic study.

EP Findings

EPS was performed in 248 patients: 206 (91%) with persistent WPW, 26 (68%) with intermittent WPW, and 16 (53%) with loss of preexcitation on Holter/exercise testing (Table IV). There was a similar proportion of patients with inducible tachycardia among all groups (P = 0.63). APs in patients with intermittent WPW had significantly longer median APERP (P = 0.0008) and BCLs (P = 0.0001) as compared to those with persistent WPW or loss of WPW on Holter/exercise testing. However, the frequency of high-risk pathways with an APERP, BCL, or shortest preexcited RR interval ≤250 ms was not statistically different between groups (P = 0.09) when analyzing the baseline (off isoproterenol) data. When including isoproterenol information in the definition of high risk, the percentage of patients with high-risk pathways was then highest among those with loss of preexcitation on Holter/exercise testing: 54%, versus 16% with persistent WPW and 11% with intermittent WPW (P = 0.005). Only a limited number of patients were evaluated on isoproterenol. No patients with intermittent WPW had induced atrial fibrillation during their EPS, so all patients in this group were only deemed high risk by APERP and/or BCL criteria. In the subgroup of intermittent WPW patients who were asymptomatic (n = 7), none had high-risk pathways based on the APERP or BCL criteria. There were two asymptomatic patients with loss of preexcitation on Holter/exercise testing whose pathway was deemed high risk.

Among patients with persistent WPW by pre-EPS ECG, 90% displayed persistent WPW throughout the EPS, whereas smaller percentages

were found to have fascicular fibers (5%), no apparent AP (2%), intermittent conduction (2%), or a concealed pathway (1%). There were five patients with persistent preexcitation who were found to have no AP on EPS: three with only subtle preexcitation on pre-EPS ECGs as interpreted by a cardiologist (in effect, false positive readings), one with clear preexcitation by ECG but no preexcitation throughout the entire EPS or on a follow-up ECG, and one with supraventricular tachycardia and subtle preexcitation on baseline ECG but who was found to have atrioventricular nodal reentrant tachycardia (no AP) on EPS.

Of patients who underwent EPS, ablation was performed in 86% with persistent WPW, 73% with intermittent WPW, and 88% with loss of preexcitation on exercise testing/Holter ($P = 0.23$; Table IV). Reasons for not performing an ablation were either attending discretion that a particular pathway was nonmalignant or findings of a fascicular fiber or no pathway apparent during the EPS. Distribution of pathway locations did not differ between groups. Of the patients with intermittent WPW who were at high risk by EP criteria, one had a left lateral pathway and one had a posteroseptal pathway. When attempted, ablation was successful in 95% of persistent WPW patients and 100% of those with intermittent WPW or loss of preexcitation on Holter/exercise testing ($P = 1.00$). There was no difference in the proportion of patients who underwent radiofrequency ablation versus cryoablation ($P = 0.33$).

Complications of ablation were rare in all groups. One patient with intermittent WPW developed a persistent migraine headache immediately postanesthesia. Among patients with persistent WPW, one had impaired lower extremity perfusion during EPS secondary to arterial placement of two wires, which were removed with restoration of normal pulses and perfusion by the end of the procedure; one developed a pseudoaneurysm at site of groin catheter insertion, which was successfully treated with a single thrombin injection, and one sustained a corneal abrasion that resolved with erythromycin ointment. There were no transient or permanent AV nodal injuries sustained during ablation.

Discussion

Our principle findings are in keeping with the only other published study to our knowledge comparing children with intermittent versus persistent preexcitation. Although patients with intermittent preexcitation had a longer median APERP, they had no difference in the frequency of high-risk APs by EP criteria as compared to those with persistent WPW. Interestingly, patients with loss of preexcitation on exercise testing or Holter monitoring did have a higher frequency of high-risk pathways, but only when considering testing both on and off of isoproterenol. There were no differences between groups in the frequency of high-risk pathways when examining data only off of isoproterenol. It should be noted, however, that only a small subset of patients were tested on isoproterenol, so it is unclear if this finding can be generalized to other groups of patients. Symptoms also did not differ between groups. A very small number of patients in any group experienced preexcited atrial fibrillation, and no patients had a sudden cardiac arrest that was clearly attributable to WPW.

To our knowledge, there is only one similar study in pediatric patients with intermittent WPW. In a single-center retrospective review that included only patients who proceeded to EPS, Mah et al. found that while patients with intermittent WPW had a longer median APERP, the frequency of high-risk pathways between groups did not differ significantly.[7] It is important to note that they used the same definition of a high-risk pathway as did this study (APERP or shortest preexcited RR interval during atrial pacing <250 ms); Mah et al. also found no difference between groups in the incidence of retrograde conduction or inducible tachycardia. Interestingly, since all of their patients with intermittent WPW and high-risk pathways were found to have left lateral pathways, they note it is possible that longer intraatrial conduction times may have intermittently masked the delta wave at baseline. In this study, one pathway in this subgroup of patients was left lateral and one was posteroseptal, so it is unclear if this phenomenon could have been at play in this study, as well.

Regarding clinical presentation, Mah et al. found a significantly higher percentage of intermittent WPW patients to be symptomatic prior to EP study.[7] However, this may have represented a selection bias in that asymptomatic patients with intermittent WPW may have been less likely to be referred to EP study, particularly in light of the most recent PACES/HRS recommendations.[6] This study included all patients with ventricular preexcitation and found no significant differences between groups regarding symptoms at presentation or symptoms developed throughout their course of follow-up. These findings were also mirrored in the subgroup of patients who did not undergo EPS, although it is difficult to draw strong conclusions from this subgroup as their length of follow-up was shorter than the included population as a whole. With regard to patients with intermittent WPW and who were asymptomatic, both Mah et al. and our data show that all patients in this category (intermittent WPW

and no symptoms) were found to have low-risk conduction properties of the AP by invasive EP study. Although the patient numbers were small (n = 5 in Mah study and n = 7 in our study), the data would support the approach to asymptomatic WPW patients as outlined by the HRS/PACES consensus statement.[6,7]

Much literature has focused on risk-stratifying patients with WPW in order to determine which patients should undergo invasive EPSs and possible ablation procedures. Loss of preexcitation with exercise testing has relatively poor specificity and sensitivity for predicting which APs will have a shortest preexcited RR interval <250 ms, although these can be improved with the addition of disopyramide testing.[8] Similarly, symptoms in children with persistent preexcitation may be suboptimal predictors of risk. In a retrospective review of 60 children with WPW, 35% who were considered "low risk" at presentation by virtue of having supraventricular tachycardia but no history of syncope, atrial fibrillation, or cardiac arrest were found to have high-risk pathways based on a preexcited RR interval <220 ms.[9] Furthermore, of the 10 patients who presented in cardiac arrest, 90% had no preceding symptoms prior to arrest. Another study of 119 children with WPW who underwent EPS found no difference in APERP, presence of multiple APs, or tachycardia inducibility between patients who presented with syncope, documented SVT, or no symptoms.[10] Additionally, 9% of asymptomatic patients had high-risk pathways with APERP <240 ms. Furthermore, multiple case reports in adults have documented high-risk APs and preexcited atrial fibrillation with rapid ventricular conduction in patients with intermittent WPW.[11–15] Further studies are therefore needed to more accurately risk stratify patients based on their symptomatology and the intermittency versus persistence of their APs.

The definition of high-risk AP has traditionally been baseline conduction values without the added information from the administration of isoproterenol during invasive electrophysiology testing. Prior studies would suggest that the use of isoproterenol likely increases the sensitivity to detect patients with high-risk pathways but at the cost of reduced specificity.[16,17] In our study, only 8–10% of each group was tested with the administration of isoproterenol. We would have expected a similar increase in high-risk pathway designation in each group. We cannot fully explain, therefore, the finding that the patients with intermittent preexcitation on exercise testing or Holter monitoring had a higher frequency of high-risk pathways if defined as including data both at baseline and on isoproterenol (but not when baseline values alone were analyzed). Perhaps there was a dose effect that was not accounted for in this study.

These findings may justify renewed consideration as to whether invasive EPS should be more broadly pursued in patients with intermittent WPW, particularly those who are symptomatic. Two studies have now demonstrated that there is no significant difference in the frequency of high-risk pathways in intermittent versus persistent WPW.[7] In both studies, however, no patients with intermittent WPW who were asymptomatic were found to have a high-risk AP, lending support to the current PACES/HRS guidelines. While this study employs a commonly used definition of a high-risk pathway as having an APERP, BCL, or shortest preexcited RR interval in atrial fibrillation <250 ms, the overall rate of sudden death or other adverse clinical events has been very low in this study and the prior of intermittent WPW in children.[7] No prior studies on the natural history of WPW in children have separated those with intermittency.[3,18–20] Intermittent WPW is a relatively common clinical scenario for pediatric electrophysiologists, as the prevalence of intermittency in patients with WPW has ranged from 7% to as high as 50% in prior case series and meta-analyses,[1,16,21–24] so it will be important to continue to investigate long-term outcomes in these patients in order to better weigh the risks and benefits of invasive testing and ablation.

Limitations

Limitations inherent in this study include its retrospective design and moderate-sized patient sample from a single institution. Additionally, the 2012 PACES/HRS consensus statement for asymptomatic WPW patients uses a shortest preexcited cycle length during atrial fibrillation in its definition of high-risk pathways, with BCL mentioned as a reasonable alternative. The majority of patients included in this study did not have atrial fibrillation induced during EPS, as this was performed only at attending physician discretion and not part of the standard protocol for all patients. Therefore, we can make no comparison of the shortest preexcited cycle length during atrial fibrillation between groups, but we do include BCL as a similar definition of minimum cycle length during preexcitation. This study's definition of high risk, however, is broader as it includes APERP in addition.

Conclusion

As compared to patients with persistent WPW, those with intermittent WPW are equally likely to have high-risk APs as defined by an

APERP, BCL, or shortest preexcited RR interval ≤250 ms. Larger scale, multiinstitution studies with longer follow-up are warranted to validate these findings, particularly in light of the relatively low incidence of clinically relevant adverse events in children.

References

1. Klein GJ, Galamhusein SS. Intermittent preexcitation in the Wolff-Parkinson-White syndrome. Am J Cardiol 1983; 52:292–296.
2. Pappone C, Vicedomini G, Manguso F, Baldi M, Pappone A, Petretta A, Vitale R, et al. Risk of malignant arrhythmias in initially symptomatic patients with Wolff-Parkinson-White syndrome. Circulation 2012; 125:661–668.
3. Santinelli V, Radinovic A, Manguso F, Vicedomini G, Gulletta S, Paglino G, Mazzone P, et al. The natural history of asymptomatic ventricular pre-excitation. J Am Coll Cardiol 2009; 53:275–280.
4. Santinelli V, Radinovic A, Manguso F, Vicedomini G, Ciconte G, Gulletta S, Paglino G, et al. Asymptomatic ventricular preexcitation: A long-term prospective follow-up study of 293 adult patients. Circ Arrhythmia Electrophysiol 2009; 2:102–107.
5. Pappone C, Santinelli V, Rasanio S, Vicedomini G, Nardi S, Pappone A, Tortoriello V, et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff-Parkinson-White pattern. J Am Coll Cardiol 2003; 41:239–244.
6. Cohen MI, Triedman JK, Cannon BC, Davis AM, Drago F, Janousek J, Klein GJ, et al. PACES/HRS expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern: Developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACE, HRS, the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), the American Academy of Pediatrics (AAP), and the Canadian Heart Rhythm Society (CHRS). Heart Rhythm 2012; 9: 1006–1024.
7. Mah DY, Sherwin ED, Alexander ME, Cecchin F, Abrams DJ, Walsh EP, Triedman JK. The electrophysiological characteristic s of accessory pathways in pediatric patients with intermittent preexcitation. Pacing Clin Electrophysiol 2013; 36: 1117–1122.
8. Sharma AD, Yee R, Guiraudon G, Klein GJ. Sensitivity and specificity of invasive and non-invasive testing for risk of sudden death in Wolff-Parkinson-White syndrome. J Am Coll Cardiol 1987; 10:373–381.
9. Bromberg BI, Lindsay BD, Cain ME, Cox JL. Impact of clinical history and electrophysiologic characterization of accessory pathways on management strategies to reduce sudden death among children with Wolff-Parkinson-White syndrome. J Am Coll Cardiol 1996; 27:690–695.
10. Dubin AM, Collins KK, Chiesa N, Hanisch D, VanHare GF. Use of electrophysiologic testing to assess risk in children with Wolff-Parkinson-White syndrome. Cardiol Young 2002; 12: 248–252.
11. Aleong RG, Singh SM, Levinson JR, Milan DJ. Catecholamine challenge unmasking high-risk features in the Wolff-Parkinson-White syndrome. Europace 2009; 11:1396–1398.
12. Medeiros A, Iturralde P, Guevara M, Mendoza C, Colin L. Sudden death in intermittent Wolff-Parkinson-White syndrome. Arch Cardiol Mex 2001; 71:59–65.
13. Gemma LW, Steinberg LA, Prystowsky EN, Padanilam BJ. Development of rapid preexcited ventricular response to atrial fibrillation in a patient with intermittent preexcitation. J Cardiovasc Electrophysiol 2013; 24:347–350.
14. Kim RJ, Gerling RJ, Kono AT, Greenberg ML. Precipitation of ventricular fibrillation by intravenous diltiazem and metoprolol in a young patient with occult Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol 2008; 31:776–779.
15. Kadoya T, Seto A, Aoyama K, Takenaka I. Development of rapid atrial fibrillation with a wide QRS complex after neostigmine in a patient with intermittent Wolff-Parkinson-White syndrome. Br J Anaesth 2009; 83:815–818.
16. Moore JP, Kannankeril PJ, Fish FA. Isoproterenol administration during general anesthesia for the evaluation of children with ventricular preexcitation. Circ Arrhyhtm Electrophysiol 2011; 4:73–78.
17. Yamamoto T, Yeh SJ, Lin FC, Wu DL. Effects of isoproterenol on accessory pathway conduction in intermittent or concealed Wolff-Parkinson-White syndrome. Am J Cardiol 1990; 65:1438–1442.
18. Fazio G, Mossuto C, Basile I, Gennaro F, D'Angelo L, Visconti C, Ferrara F, et al. Asymptomatic ventricular pre-excitation in children. J Cardiovasc Med 2009; 10:59–63.
19. Pappone C, Manguso F, Santinelli R, Vicedomini G, Sala S, Paglino G, Mazzone P, et al. Radiofrequency ablation in children with asymptomatic Wolff-Parkinson-White syndrome. N Engl J Med 2004; 351:1197–1205.
20. Pappone C, Santinelli V, Manguso F, Augello G, Santinelli O, Vicedomini G, Gulletta S, et al. A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff-Parkinson-White syndrome. N Engl J Med 2003; 349:1803–1811.
21. Munger TM, Packer DL, Hammill SC, Feldman BJ, Ballard DJ, Holmes DR Jr., Gersh BJ. A population study of the natural history of Wolff-Parkinson-White syndrome in Olmsted County, Minnesota, 1952–1989. Circulation 1993; 87:866–873.
22. Tseng CD, Tseng YZ, Lo HM, Chiang FT, Hsu KL, Wu TL. Holter monitoring in patients with Wolff-Parkinson-White syndrome: With special reference to intermittent preexcitation. J Formos Med Assoc 1992; 91:52–56.
23. Lee PC, Hwang B, Chen YJ, Tai CT, Chen SA, Chiang CE. Electrophysiologic characteristics and radiofrequency catheter ablation in children with Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol 2006; 29:490–495.
24. Obeyesekere MN, Leong-Sit P, Massel D, Manlucu J, Krahn AD, Skanes AC, Yee R, et al. Incidence of atrial fibrillation and prevalence of intermittent pre-excitation in asymptomatic Wolff-Parkinson-White patients: A meta-analysis. Int J Cardiol 2012; 20:75–77.