Wolff-Parkinson-White Syndrome and Isoproterenol Testing in Children
A Valid Adjunct to Predict Risk?

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Wolff-Parkinson-White syndrome (WPW) is the most common indication for invasive cardiac catheterization and electrophysiological testing in children. There are presently 2 predominant reasons for this. First, patients with WPW are, as the original 1930 investigators so eloquently pointed out, at risk for “paroxysmal tachycardia.” Supraventricular tachycardia is typically either orthodromic or, less commonly, antidromic reentrant tachycardia and can cause recurrent and debilitating symptoms. Present-day ablation techniques provide the promise of a cure for WPW in as many as 90% to 100% of patients who undergo this procedure with relatively low risk.2,3 Multiple studies have demonstrated the many medical, psychological, and financial benefits of ablation in the symptomatic WPW child.4–6

The second reason that children with WPW undergo invasive catheterization and electrophysiological testing is to assess the risk of dying of ventricular fibrillation. The risk of sudden cardiac death in WPW in the pediatric population is, unfortunately, not known, and because of this, estimates of this risk have varied widely and range from 1% over a patient’s lifetime to 0.0015 per patient-year.7,8 The reasons for not knowing this figure are myriad but ultimately stem from an inability to adequately identify both the numerator and denominator of WPW patients when creating these sorts of calculations. However, it would be fair and true to state that most authorities believe sudden cardiac death to be a rare event in both children and adults with WPW, especially in those patients who are asymptomatic.

Thus, for the symptomatic child with WPW, most are in agreement that ablation, given the correct patient age, size, and history, is both appropriate and probably recommended in the majority of cases.9 However, the asymptomatic child with WPW poses significant problems for the pediatric electrophysiologist. In “olden times” (ie, before 2000), it was fairly common to recommend an expectant management approach to this patient population. This approach was based on a few factors. First, and most important, the risk of sudden death in the asymptomatic WPW child was believed to be low. Just how low was not well established, but it was clear both in the limited WPW natural history data as well as daily clinical practice that it was rare to see an asymptomatic WPW patient die suddenly.7,8 Second, electrophysiological studies in children were still relatively “novel,” and the risks of an invasive electrophysiological study were still not fully established but seemed, at least on the surface, to be potentially greater than the risk of sudden death. Finally, it was unclear in that era if an electrophysiological study performed on an asymptomatic WPW patient had adequate positive predictive value to identify those children at risk for sudden cardiac death. For all of these reasons, the value of invasive electrophysiological studies, which are typically performed under general anesthesia in the pediatric population, were questioned and were generally reserved for the atypical or frankly symptomatic child with WPW.

However, in the past decade, the general “perceived wisdom” of the pediatric electrophysiology community has markedly changed. Today, the vast majority of pediatric electrophysiologists recommend formal electrophysiological testing in the asymptomatic WPW child to assess risk of sudden cardiac death. In 2003, Campbell et al10 reported the results of a survey taken of experienced pediatric electrophysiologists and reported that 84% favored formal electrophysiological studies in the asymptomatic WPW child. The most compelling reason for this is the well-documented fact that sudden cardiac death, though rare in this patient population, may be the first presenting symptom of the syndrome.11 The risk of sudden unexpected death is now balanced with the knowledge that the risks of invasive electrophysiological testing are small.2 Furthermore, in the past decade, a series of articles have been published, predominantly from Italy, suggesting that the risk of sudden cardiac death in children may have been underestimated in prior research.12–14 A recent publication from Santinelli et al14 demonstrated that at a median follow-up of only 51 months, 19 of 184 (10%) children who were asymptomatic at the time of a baseline electrophysiological study had what the group referred to as a “potentially life-threatening event.” Moreover, the same group’s data suggested that the accessory pathway effective refractory period and/or presence of multiple accessory pathways were predictive of life-threatening events. It is interesting to note that despite these 19 “potentially life-threatening events,” no patient actually died during follow-up. In refer-
ence to another similar work by the same group, Triedman et al\textsuperscript{15} summarized the concerns of many in the pediatric electrophysiology community in describing what he referred to as the “extraordinarily high rate” of life-threatening events reported in the group as a whole.

With this as a backdrop, in the present edition of Circulation: Arrhythmia and Electrophysiology, Moore et al\textsuperscript{16} report on the effects of isoproterenol testing on electrophysiological findings obtained in children with WPW during formal testing under general anesthesia. Many of the different findings that have been previously demonstrated to potentially identify the “high-risk” WPW child were analyzed by the authors in this excellent retrospective review of 151 children with WPW who underwent formal intracardiac electrophysiological testing. Patients reviewed in this single-center study were a mix of both the symptomatic and asymptomatic. Previously demonstrated markers of potential “risk” such as accessory pathway effective refractory period 1:1 preexcited conduction characteristics with both atrial pacing and in atrial fibrillation, and tachycardia (orthodromic reciprocating tachycardia/antidromic reciprocating tachycardia) inducibility were assessed. The authors demonstrated that low-dose isoproterenol infusion could affect the factors that are believed to be associated with “high risk” in a very large percentage of patients (20% to 36% depending on measure assessed) changing their “risk profile” from that of “low risk” to one of “high.” They also demonstrated an inverse correlation between pathway conduction characteristics and age. Unfortunately, because a large percentage of the patients studied underwent successful ablation based, in part, on these electrophysiological findings, the reader cannot glean any information as to the predictive value of these interesting findings.

What are the lessons of these findings? The investigators suggest in this retrospective study that accessory pathways in children are quite sensitive to adrenergic stimulation and posit that isoproterenol infusion may play an important role in determining whether an accessory pathway may result in a dangerous outcome for the pediatric patient with WPW. The use of this agent may be particularly important given the fact that electrophysiological studies and risk assessment in these children are commonly performed under general anesthesia. Additionally, isoproterenol testing may also be of greater importance in the pediatric population because of the greater propensity of children to participate in high adrenergic activities versus the adult population. However, as the authors also clearly point out, though this form of testing may improve testing sensitivity, this testing may also adversely affect the specificity of results that are already unclear. Though the negative predictive value of certain electrophysiological measurements such as ventricular response rates in WPW and may point to the need for the use of isoproterenol in risk assessment, this may be reasonable. However, it is important to recall the sagacity of Mark Twain when he suggested that “To the man with a hammer, everything looks like a nail.” The risks of invasive electrophysiological study and ablation in children are low but not zero, and it is presently unknown how these compare with the risks of sudden cardiac death in the asymptomatic child with WPW. Though perhaps heretical to suggest, the benefit of this form of testing in the asymptomatic WPW child, as well as the potential benefits of isoproterenol testing during such testing, are still largely unknown as a predictor of sudden cardiac death and these facts may provide adequate rationale for proceeding with a large-scale, multicenter prospective study. Though invasive electrophysiological testing for the asymptomatic WPW patient is rapidly becoming more commonly viewed as a near “standard of care” by the majority of pediatric cardiac electrophysiologists in the present era, it would be wise to think once more of the words of Mr Twain when he wrote, “Whenever you find yourself on the side of the majority, it’s time to pause and reflect.”

Disclosures

None.

References


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