Electrophysiology Testing and Catheter Ablation Are Helpful When Evaluating Asymptomatic Patients with Wolff-Parkinson-White Pattern

The Pro Perspective

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KEYWORDS

• Wolff-Parkinson-White syndrome • Sudden cardiac death • Catheter ablation
• Electrophysiologic testing

KEY POINTS

- Ventricular fibrillation frequently occurs in young, previously asymptomatic people as the first clinical manifestation of Wolff-Parkinson-White (WPW) syndrome; many other initially asymptomatic or symptomatic people experience benign arrhythmias, recurrences, or remain asymptomatic.
- Our experience suggests that, regardless of the presence of symptoms, intrinsic electrophysiologic properties of accessory pathways predict the risk of developing malignant arrhythmias or sudden death and that electrophysiologic testing is the gold standard for stratifying the risk.
- Catheter ablation of dangerous accessory pathways can definitively eliminate the lifetime risk of sudden cardiac death in a subgroup of selected asymptomatic people, in whom ablation could reasonably be recommended as class IA, as currently recommended for all initially symptomatic patients with WPW regardless of their risk.
- We believe that, in the era of widespread use of catheter ablation, it has become unacceptable for even 1 asymptomatic individual with WPW to be at potential risk of dying unexpectedly or experiencing life-threatening arrhythmic events.

THE NATURAL HISTORY OF WOLFF-PARKINSON-WHITE SYNDROME IN THE ERA OF CATHETER ABLATION: AN EPOCHAL CHANGE

In the era of catheter ablation the management of asymptomatic patients incidentally discovered to have Wolff-Parkinson-White (WPW) syndrome on electrocardiogram (ECG) for many decades has been a controversial issue that has led to several debates at many official cardiology congresses worldwide in the last 10 years. The 2003 American Heart Association/American College of Cardiology/European Society of Cardiology guidelines considered only symptomatic WPW as a class IA recommendation for catheter ablation and

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considered asymptomatic WPW as class III (no treatment), restricting ablation only to people in high-risk occupations and professional athletes.[1] This assumption in all probability was based on the assumption that asymptomatic people with WPW are at minimal or no risk of sudden death as well as on the fact that many patients who experience ventricular fibrillation (VF) have had previous episodes of both atrial fibrillation (AF) and paroxysmal supraventricular tachycardia. Therefore, in the pre–ablation era guidelines attention was constantly focused on highly symptomatic patients with WPW, neglecting those who are initially asymptomatic. However, in the last few years in the era of catheter ablation, the results of several large prospective randomized or observational studies, most of which are from our group, have better defined the natural history of patients with asymptomatic ventricular preexcitation as well as the role of catheter ablation and the risk of sudden death.[2–10] Therefore, based on the results of these studies, the recent Pediatric and Congenital Electrophysiology Society (PACES)/Heart Rhythm Society (HRS) Expert Consensus has revised the HRS recommendations to which they consented previously, extending catheter ablation as class IIA to asymptomatic people with WPW found to be at risk after electrophysiologic testing.[11] As a result, the current 2012 PACES/HRS expert consensus statement is that invasive measurement of the shortest preexcited R-R interval (SPERRI) in AF is useful for risk stratification, and that patients with a shortest preexcited R-R interval of less than or equal to 250 milliseconds at baseline are at increased risk for sudden cardiac death (SCD).[11] Before 2002, the HRS expert consensus statement recommended ablation as a class IIB indication only for asymptomatic children with WPW aged greater than 5 years, whereas in those aged less than 5 years ablation was a class III indication.[12] The European guidelines for competitive sports eligibility also recognize the importance of performing an electrophysiologic study in all patients with asymptomatic ventricular preexcitation to identify people at risk in whom catheter ablation is recommended before allowing participation in competitive sports.[13]

Our data indicate that the natural history of WPW syndrome is much simpler than was previously thought, considering the intrinsic properties of accessory pathways as the most important predictors of the outcome regardless of the presence of symptoms. The natural history of the disease is highly variable; many initially asymptomatic patients, particularly the older ones, may remain asymptomatic over time and, similarly, many symptomatic patients never experience recurrences, malignant arrhythmias, or sudden death. Our data on the natural history of WPW syndrome show that in the asymptomatic WPW population, particularly in children or young patients, the risk of SCD is similar or even higher than in the symptomatic WPW population, essentially depending on the intrinsic electrophysiologic properties of the accessory pathways rather than on the symptoms alone,[5–8] and this has made it possible to revisit and update guidelines recommendations on the asymptomatic WPW population. The overrepresentation of young and previously asymptomatic patients in the SCD group has been confirmed by our recent experience and several other anecdotal studies. The results of our first 2008 survey, which was submitted to 111 electrophysiologists selected from the worldwide electrophysiology (EP) community, revealed that most electrophysiologists (100 out of 111) shared our point of view on asymptomatic WPW management strategy, agreeing with risk stratification by EP testing and prophylactic ablation only in selected high-risk individuals.[9] The results of a prior survey by Campbell and colleagues,[14] which was submitted to members of the PACES, showed that, of 43 responders (of whom 37 had been performing ablation for >5 years), 36 used EP testing to risk stratify children with asymptomatic WPW syndrome. Note that most (33 of 43; 77%) also performed catheter ablation in children with a shortest preexcited RR during AF of less than 240 milliseconds, and 19 of 43 (44%) would have ablated those with AP ERP less than 240 milliseconds. Only 11 of 43 (26%) would ablate those with inducible SVT alone.[14] These data taken together have strongly stimulated reconsideration of guidelines and more intensive screening programs with risk stratification by EP testing, particularly in the young asymptomatic WPW population, as recently reported by 2 European surveys.[15,16]

WHY IS IT NECESSARY TO PERFORM ELECTROPHYSIOLOGIC TESTING AND CATHETER ABLATION IN THE WOLFF-PARKINSON-WHITE POPULATION?

WPW syndrome is associated with recurrent arrhythmias and a low but lifetime risk of cardiac arrest or SCD, so the ultimate goal of catheter ablation should be to prevent SCD and improve quality of life. In the incidentally discovered asymptomatic WPW population, the ultimate goal of catheter ablation is to prevent SCD because it can be the first clinical manifestation of the syndrome in many previously asymptomatic young people. If the end point of ablation

is definitive elimination of the lifetime risk of SCD, it is unclear why catheter ablation is recommended as class IA in all symptomatic patients, many of whom are initially symptomatic patients with just an episode of SVT and minimal or no risk of SCD.

Our experience and that of other investigators have provided additional data indicating that the risk of sudden death can be even higher in asymptomatic children or the young WPW population and that only the intrinsic electrophysiologic properties of accessory pathways can predict this risk.[5,6] The main difference between our results and prior anecdotal natural studies considering asymptomatic WPW syndrome as a benign condition is the intensity of monitoring and the presence of atypical symptoms in children, which can frequently be dismissed as being noncardiac. In agreement with our conclusions are the results of a recent retrospective study among 124 consecutive children with ventricular preexcitation, of whom 51 were symptomatic and 73 were asymptomatic, which concluded that symptomatic and asymptomatic children have the same potential risk of SCD.[17] These new data have important clinical implications because, in the era of the widespread use of radiofrequency ablation (RFA), it is easier to make decisions on prevention, particularly in the initially asymptomatic population. Considering the potential, albeit very rare, complication rates of electrophysiologic testing as currently reported worldwide,[18] the choice to provide RFA or not after EP testing should be based on the presence of dangerous accessory pathways and not exclusively on the presence of symptoms, as currently recommended. The accumulating clinical evidence for many years worldwide clearly shows that malignant arrhythmias, aborted SCD, and sudden death can be the first clinical manifestations of the syndrome in many previously asymptomatic people, representing a tragic unpredictable event, particularly in the young asymptomatic population.[1–10,19–21] Therefore, in the current era of widespread use of catheter ablation all clinicians should attempt to prevent such tragic events, particularly in initially asymptomatic children or young people, by more intensive screening programs; current expert recommendations agree with our point of view. At present, it is estimated that most adolescents (≈65%) with a WPW pattern on a resting ECG are asymptomatic. ECG recordings by recent intensive screening programs before sports participation or before medical and surgical procedures have identified an increasing number of asymptomatic individuals with a WPW ECG pattern who are increasingly referred to EP laboratories worldwide for EP testing and risk stratification.

CATHETER ABLATION IN SELECTED ASYMPTOMATIC PATIENTS WITH WOLFF-PARKINSON-WHITE

In the last 10 years, many large prospective observational and randomized electrophysiology-guided studies have been published by our group on the natural history and treatment of the asymptomatic WPW population. The first was a prospective study of 212 initially asymptomatic adult patients of whom 33 became symptomatic over a 5-year period.[4] They showed shorter APERP at baseline (246 vs 283 milliseconds) and during isoproterenol infusion (203 vs 225 milliseconds). The association of short APERP and inducibility of SVT showed a positive predictive value of 47% with a negative predictive value of 97% for subsequent arrhythmic events. There were 3 asymptomatic patients with an APERP less than 200 milliseconds and an SPERRI less than 230 milliseconds who developed VF. In another study, both clinical and electrophysiologic data were collected in 184 asymptomatic children with ventricular preexcitation during a median follow-up of 5 years.[8] Compared with subjects who remained asymptomatic, the 51 patients who became symptomatic during the follow-up had significantly different EP parameters, such as an APERP less than 240 milliseconds (89% vs 17%), multiple accessory pathways (47% vs 6.0%), and an intact atrioventricular (AV) reentrant supraventricular circuit (84% vs 23%). Three patients experienced a resuscitated cardiac arrest caused by VF preceded by preexcited AF with rapid ventricular response immediately before (1 patient) or at hospital admission (2 patients). All 3 showed high-risk accessory pathway electrophysiologic characteristics at the baseline EP study (APERP <220 milliseconds and SPERRI <200 milliseconds), and all subsequently underwent successful catheter ablation. In a more recent long-term follow-up study, we compared the outcomes of symptomatic and asymptomatic untreated patients with WPW with similar baseline electrophysiologic characteristics.[5] Over an 8-year follow-up period, only 2 of 451 symptomatic patients (0.4%) experienced cardiac arrest, whereas as many as 13 of 550 initially asymptomatic patients (2.4%) had cardiac arrest as the first clinical manifestation of the syndrome, but none of them died. In this study, subjects who developed VF had a characteristic electrophysiologic profile. Compared with patients experiencing malignant arrhythmias, they showed more inducible

preexcited sustained AF triggered by AV reciprocating tachycardia (73.3% vs 44.9%) and shorter median accessory pathway AERP (220 vs 240 milliseconds). A posteroseptal location of accessory pathways was found in almost all patients with VF, whereas the rate of multiple accessory pathways was similar in patients with VF or malignant arrhythmias, as reported by Timmermans and colleagues.[19] Note that Kaplan-Meier estimates showed that, over the 8-year follow-up period, asymptomatic individuals were more likely to experience VF than the symptomatic individuals. Multivariable analysis showed that the presence of symptoms was not an independent risk factor of outcome, whereas shorter accessory pathway AERP and AV reciprocating tachycardia triggering AF were associated with VF or malignant arrhythmias. Analysis of time-dependent receiver operating curves for the prediction of VF showed an optimal accessory pathway AERP cutoff point at 240 milliseconds, which confirms the key role of a very short effective refractory period of the accessory pathway to facilitate degeneration of AF into VF. Taken together, these data, although confirming an overall very low annual rate of VF in the WPW population, report higher rates in asymptomatic patients with WPW, predominantly in the pediatric population. These seminal observations strongly suggest that, after electrophysiologic testing and in a minority of asymptomatic high-risk patients, catheter ablation is appropriate and should be recommended as class IA, as currently recommended for all symptomatic patients regardless of the accessory pathway properties.

ELECTROPHYSIOLOGIC TESTING AND RISK STRATIFICATION IN THE ASYMPTOMATIC WOLFF-PARKINSON-WHITE POPULATION

In current practice, the intent of risk stratification in asymptomatic patients with a WPW ECG pattern is to identify the individuals who are at risk for a lethal cardiac arrhythmia. Our data confirm that the critical obligatory condition for VF is the presence of rapid preexcited AF and a short anterograde functional refractory period of the accessory pathway as reflected in the shortest R-R interval between preexcited beats in AF. Invasive EP testing should include measurement of the shortest preexcited R-R interval during induced AF in addition to determination of the number and location of accessory pathways, the anterograde and retrograde characteristics of the accessory pathways and AV node, and the effective refractory period of the accessory pathway and of the ventricle at multiple cycle lengths.

PREDICTORS OF THE RISK OF SUDDEN DEATH IN THE ASYMPTOMATIC WOLFF-PARKINSON-WHITE POPULATION

Despite SCD being the first clinical presentation in many previously asymptomatic children or young people with WPW ECG, for several decades the asymptomatic WPW population has been considered to be at minimal or no risk of sudden death, and catheter ablation to prevent sudden death has not been recommended by guidelines.[1] Noninvasive risk stratification with Holter monitoring, exercise stress testing, and pharmacologic testing can be performed before invasive studies are considered,[17] but sensitivity and specificity of noninvasive testing has been shown to be poor. In WPW syndrome, invasive electrophysiologic testing is considered the gold standard for risk stratification; transesophageal testing is not accurate enough to evaluate the intrinsic electrophysiologic properties of accessory pathways, particularly in patients with multiple bypass tracts. In addition, AF inducibility is not reproducible and this semi-invasive procedure is not risk free because high-output pacing is frequently required to activate the atrium from the esophagus, which can be painful, requiring the use of heavy sedation.[22] Risk stratification by independent predictors requires a well-defined end point of outcome, such as malignant arrhythmias/VF, and, most importantly, the need of an adequate number of events for a multivariate analysis, which in a patient population presumed to be at low risk requires a large number of enrolled patients with intensive and adequate lengths of follow-up to detect potentially rare events. To date, only a few natural history studies on the asymptomatic WPW population have fulfilled these criteria, and the results have recently been published from our group.[7,8] Multivariate analysis showed that short anterograde ERP of the AP (<240 milliseconds) and multiple accessory pathways are able to predict the occurrence of malignant arrhythmias and VF. We also showed for the first time that the risk of malignant arrhythmias and/or SCD can be higher in the asymptomatic pediatric population, beginning early in life[7] and decreasing over time with minimal or no risk in adults,[8] which confirms the results of previous anecdotal follow-up and electrophysiology-guided studies reporting minimal or no risk of SCD in the adult WPW population. Because many of the reported risk factors cannot be adequately identified without prior invasive electrophysiologic testing, we are in favor of routine EP testing to assess risk, with subsequent ablation in patients identified to have these risk factors. The major message from our experience

is that the natural history of asymptomatic young people with WPW is not benign and that EP testing provides excellent risk stratification to identify those at risk of having dangerous accessory pathways. Patients who are noninducible with a long APERP can be followed without treatment, but those who are inducible or have a short AP ERP should be considered for ablation. We completely agree with the editorial comment of Balaji[23] about our study[8] that one impediment to settling the controversy about the management of asymptomatic WPW in children was ignorance about the natural history of asymptomatic WPW from childhood to adulthood.

THE IMPACT OF RADIOFREQUENCY ABLATION ON THE NATURAL HISTORY OF WOLFF-PARKINSON-WHITE SYNDROME

Since the introduction of RFA in the early 1990s, the procedure has revolutionized the approach to the management of WPW syndrome, becoming the method of choice potentially available to all patients with WPW to definitively eliminate benign or dangerous accessory pathways with their intrinsic risks. As a result, the approach to the asymptomatic WPW population has now been significantly influenced by the widespread availability of RFA. However, EP testing and RFA are invasive procedures with a potential for complications that could be unacceptable for the asymptomatic patient population, which has been erroneously supposed to be at no risk of sudden death. In a recent study from our group, a total of 1168 symptomatic or asymptomatic patients underwent RFA and 1001 additional patients with WPW with similar electrophysiologic characteristics did not.[5] The long-term results showed that there was a striking difference in outcomes between ablated and nonablated patients because, over the 8-year follow-up, no patients after RFA experienced malignant arrhythmias or VF. Note that the high success rates after RFA were associated with low rates of minor complications.[5] Therefore, the current reluctance to routinely undertake invasive EP testing for risk stratification, and the subsequent use of prophylactic ablation to prevent future arrhythmic events, are not fully justified by the potential risks of an ablation procedure. It is generally accepted that these risks are highest in small children (<4 years of age or <15 kg in weight). We believe that, in children more than 10 years of age with persistent preexcitation but without symptoms, continuing such a cautious approach can be questioned. Current data on the efficacy and safety of RFA across all locations of APs confirm the significant increase in ablation success rates from 90% in the early era to greater than 95% in the later era of RFA without major complications, as recently reported by many EP laboratories worldwide.[18]

SUMMARY

The natural history of the asymptomatic WPW population has now been more accurately defined and established. VF can frequently occur in young, previously asymptomatic people as the first clinical manifestation of the syndrome. By contrast, many other initially asymptomatic or symptomatic people may experience benign arrhythmias or recurrences, or may remain asymptomatic. Our experience suggests that, regardless of the presence of symptoms, intrinsic electrophysiologic properties of accessory pathways predict the risk of developing malignant arrhythmias or sudden death and that electrophysiologic testing is the gold standard to stratify the risk. Catheter ablation of dangerous accessory pathways can definitively eliminate the lifetime risk of SCD in a subgroup of selected asymptomatic people in whom ablation could reasonably be recommended as class IA, as currently recommended for all initially symptomatic patients with WPW regardless of their risk. We believe that, in the era of widespread use of catheter ablation, it has become unacceptable that even 1 asymptomatic individual with WPW at potential risk continues to die unexpectedly or to experience life-threatening arrhythmic events.

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