WPW Pattern in the Asymptomatic Individual
Has Anything Changed?

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The patient with the Wolff-Parkinson-White (WPW) ECG pattern has much in common with patients with other entities, such as long-QT syndrome and Brugada syndrome, which are associated with an identifying abnormality on ECG. All are relatively benign in the majority of afflicted individuals but nonetheless carry a risk of unexpected sudden death, which begs for some attempt at risk management. The WPW pattern differs from the others in that a highly effective curative procedure is available, albeit with some risk, leaving us with a decision to manage expectantly or intervene.

The WPW pattern is relatively common and found in the range of 2 to 4 individuals per 1000, the great majority of whom will never be aware of the issue unless it is discovered incidentally. The lifetime risk of mortality related to this in asymptomatic individuals can never be accurately known but has been estimated to be in the range of 1 per 1000 (0.1% annual risk). This small risk of sudden death is thought to be more “front loaded” in the first part of life, with the majority of patients identified between the ages of approximately 10 to 40 years. The small hearts of normal infants and smaller children are probably more resistant to sustained atrial fibrillation (AF) or ventricular fibrillation (VF), whereas the risk in older individuals who have not had arrhythmia is attenuated by the tendency of accessory pathways to lose their arrhythmogenic functionality over time. This relatively low mortality is supported by available postmortem studies in individuals with unexpected sudden death. The majority of these are related to unrecognized structural heart disease, but series invariably include a small percentage in whom a cause of death cannot be determined, typically in the range of 10%. This would include individuals with unrecognized long-QT syndrome, Brugada syndrome, other repolarization syndromes, idiopathic VF, short-QT syndrome, and surely others. One can reasonably speculate that unrecognized WPW (identified pathologically only with intensive efforts) forms some percentage of this group, a portion that is difficult to quantify but arguably unlikely to be the dominant portion.

The mechanism of sudden death in most patients with WPW is probably the occurrence of atrial fibrillation with a very rapid ventricular rate that can lead to ventricular fibrillation. The trigger for atrial fibrillation in healthy individuals who might be expected to have a low rate of AF is generally an episode of supraventricular tachycardia, the latter well shown to be associated with VF in survivors of arrest and induction of which is also predictive of clinical symptoms in some asymptomatic individuals. Risk factors for VF have been suggested and include the occurrence or inducibility of supraventricular tachycardia, multiple accessory pathways and a short anterograde refractory period of the accessory pathway allowing a rapid ventricular response in AF. Nonetheless, it is clear that the only essential and key factor for VF is the ability of the accessory pathway to conduct rapidly to the ventricles. This is best measured by the shortest and average preexcited intervals during atrial fibrillation or alternatively by the effective refractory period of the accessory pathway.

In this issue of *Circulation: Arrhythmia and Electrophysiology*, Santinelli et al describe the follow-up of 293 asymptomatic adults with the WPW ECG pattern who underwent electrophysiological (EP) testing without ablative intervention. The primary end point of this prospective study was the occurrence of a first arrhythmic event. Thirty-one patients had an arrhythmic event, and 17 had a “potentially” life-threatening event (AF with mean rate ≥250±18 per minute). The latter could be predicted by multivariate analysis using a combination of age, inducibility of tachycardia (atrioventricular reciprocating tachycardia in 14 and AF in 2), and effective refractory period of the accessory pathway ≤250 ms. The authors conclude that the risk of sudden death in the asymptomatic individual with WPW is “indeed small.” They also conclude that the combined features of younger age, short antegrade effective refractory period of the accessory pathway, and inducible arrhythmia accurately predict the individual destined to have an end point and suggest that this would be a suitable strategy for dealing with such individuals going forward.

It must be stated at the outset that the authors are to be commended for performing a natural history study in the ablation era and resisting what must have been an enormous temptation to act on the results of testing. It is the latest and largest natural history study examining the value of EP testing in this context. One can certainly agree with their primary conclusion that the natural history of the asymptomatic individual is indeed benign in general, in line with previous observations in the literature. However, signif-
icant issues open to controversy relate to the need to perform an electrophysiology study to obtain the variables, the selection of clinically meaningful and appropriate end points in the study, and the conclusion that meaningful risk stratification can be performed to guide who should undergo prophylactic ablation when all is said and done.

Although invasive EP testing most accurately assesses the EP properties of the accessory pathway, many noninvasive and minimally invasive techniques exist and these can be very useful for risk stratification.\textsuperscript{13–17} The mere observation of intermittent loss of the preexcitation pattern in a Holter monitor or serial ECGs for example essentially ensures that the accessory pathway has a low "margin of safety" for conduction and hence likely to block during AF, resulting in a slow ventricular response.\textsuperscript{18} There is no disagreement that EP testing is the most direct route to this information, but this is in itself not without some risk albeit small. Once EP testing is done, there is an enormous temptation to ablate the accessory pathway and the criteria for ablation will not be black and white. One can expect at least one third of patients or more to have a sufficiently short ERP to cause some concern.\textsuperscript{9, 10} In fact, the addition of isoproterenol to the baseline study may shorten the ERP of the accessory pathway to levels of potential concern in the majority of individuals with WPW.\textsuperscript{19} This is after all the final common pathway to VF and difficult to ignore regardless of the other criteria (age, inducibility) suggested by the authors in this study. Inducibility itself is not necessarily reproducible over time, and the probability of developing primary AF or AF attributable to some environmental or pathological factor (such as alcohol or hypertension) will only increase with time. It seems likely that the die will be cast to ablate much of the time once the EP study is done regardless of other risk factors, unless the ERP of the pathway is sufficiently long to reassure the physician that it will not come back to haunt at a later age.

It should be clear to all, as it certainly was to the authors of this article, that sudden death as an end point is not feasible because of the very low incidence of this complication. Even with the surrogate end point chosen, the event rate was sufficiently low to challenge the robustness of the statistical analysis. Are there clinically meaningful surrogate end points? Certainly an end point of "first arrhythmia" is measurable but perhaps not sufficient justification to allow EP testing of all individuals. One can ask whether the thoughtful clinician loses sleep worrying about the patient coming back for treatment of new supraventricular tachycardia? The concept of potentially "life-threatening" arrhythmia seems to be closer to the mark because atrial fibrillation is known to be the usual precursor of VF. Nonetheless, it is indeed striking that nobody in this study died. Indeed, we find the same striking theme in other similar studies where the occurrence of "potentially" life threatening arrhythmia far exceeds the actual mortality observed.\textsuperscript{9,10,12,20} This is very noteworthy and raises the possibility that simply raising the issues with the patient and following them helps alert them to warning arrhythmias, prompting them to seek attention appropriately. Additionally, one might also suppose that patients without cardiac disease will tolerate relatively rapid rates, providing the time to seek help if they recognize that they are having an arrhythmia.

This is a well-executed study, but data are always open to interpretation and will be in the "eye of the beholder." One might encapsulate an alternate interpretation as follows:

1. A total of 293 adult patients underwent EP study and were followed for a median of 67 (8 to 90) months.
2. A total of 31 patients developed arrhythmias and were appropriately treated.
3. No patient died.

Might one then reasonably conclude that this study in fact demonstrated the futility of EP testing in improving outcomes?

In the final analysis, the only meaningful end point that is relevant is sudden death. Fortunately, this is very rare, as the authors have clearly verified. Looking for risk factors, if one considers sporadic sudden death as the only relevant end point, is clearly futile. The era of ablation has made ablation of accessory pathways safe and accessible for many individuals. Yet complications such as AV block, stroke, tamponade, and even death have been reported\textsuperscript{21–24} and are likely underreported in the "real world." It is not difficult to envisage a small potential mortality benefit, if present, erased or eclipsed by a small complication rate if thousands of patients with pathways in various locations undergo ablation.

Should these data alter the clinical management of the asymptomatic individual with WPW or encourage a more aggressive screening of the general population? Not in our view. Recent SVT guidelines\textsuperscript{25} of the American College of Cardiology, American Heart Association, and European Society of Cardiology assign catheter ablation in the asymptomatic individual with the WPW pattern a class 2A designation. This means essentially that it is "reasonable" to offer ablation in selected patients but is not aggressively mandated in all comers by the preponderance of data showing improved outcomes. A reasonable properly informed patient might elect to pursue a strategy of follow-up with ECGs and reevaluation at selected intervals with a high degree of suspicion for new arrhythmia symptoms. On the other hand, this same individual may reasonably elect to undergo EP study with a view to ablation, finding the very small procedural risk more palatable to their circumstances than the small risk of fatal arrhythmia played out over a longer time frame. Some individuals in certain occupations (eg, military, aviation, police, competitive athletics) may find even a small risk of sudden arrhythmia unacceptable and will opt for ablation.

The choice is individualized, and the current guidelines support a thoughtful free choice by the well-informed patient. Until we can guarantee an ablation procedure without risk, this may be as good as it gets.

Disclosures

None.

References


KEY WORDS: Wolff-Parkinson-White syndrome ■ electrophysiology ■ tachyarrhythmias ■ ablation