The Asymptomatic Wolff-Parkinson-White Patient
Time to Be More Proactive?

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It is well known by now that sudden cardiac death (SCD) may occur even in the asymptomatic individual with Wolff-Parkinson-White (WPW) pattern. This is related to the occurrence of atrial fibrillation with a rapid ventricular response leading to ventricular fibrillation (VF). The essential and critical risk factor is the presence of an accessory pathway(s) (AP) with critically short antegrade refractoriness. The most common numeric in the literature reflecting this is the shortest RR interval between preexcited cycles <250 ms (SPRRI) in atrial fibrillation. The risk of SCD in the individual with asymptomatic WPW has been estimated to be low, in the range of 0.05% to 0.2% per year,1 a risk that can obviously be eliminated with successful, uncomplicated catheter ablation. These facts are not in dispute. The controversy that remains is related simply to the fact that population-wide electrophysiological assessment and ablation cannot be performed without risk of complications and even mortality that can mitigate the benefit, and broad screening and electrophysiological based management would be very costly.2 Current guidelines reflect this1 by suggesting that electrophysiological assessment with a view to ablation is reasonable when a well-informed patient chooses the small risk of ablation over a small risk due to the natural history (2A recommendation) depending on their individual circumstances. Furthermore, there is little advocacy in the guidelines for large-scale population screening. Do we now have evidence to support improved clinical outcomes for electrophysiological assessment with a view to ablation in all individuals with the WPW pattern in the general population?

The data presented in the article, “The natural history of WPW syndrome in the era of catheter ablation, insights from a registry study of 2169 patients,” by Pappone et al.,4 in the current issue of Circulation, demonstrate the outcomes in 1001 WPW patients (550 asymptomatic and 451 symptomatic) who had undergone electrophysiology testing and were followed without ablation. The authors contend that the management of asymptomatic WPW is based on the perceived influence of symptoms on prognosis and raise the notion that symptomatic status unduly influences the management of the asymptomatic individual. In reality, the management of the symptomatic individual is not related to the management of the asymptomatic individual, because the former is done primarily for symptom control with the benefit abundantly clear, whereas the latter would be done purely to prevent SCD, an unproved hypothesis. Thus, the presented symptomatic control group has no relevance to the discussion of the asymptomatic individual, and one may well consider this as a typical “attacking of a straw man.” The supremacy of AP conduction properties prognostically is hardly a new concept. Furthermore, the symptomatic patients in this study had refused ablation after electrophysiological assessment for a variety of reasons not clarified, but they were arguably informed by knowledge of AP refractoriness and accordingly cannot be truly considered as even representing the “natural history” of the WPW patient with symptoms. The relevance and validity of this group as a comparator with asymptomatic individuals with WPW is at best questionable, and we will focus most of our comments on the asymptomatic group, which is really at the heart of any management controversy in this syndrome.

VF occurred in 15 patients of whom 13 were grouped as asymptomatic, all were between 10 and 14 years of age, with a mean age of 11 years (2.4% over a median of 75 months, a crude estimate of 0.38% per year). Although it is well appreciated that VF is not a trivial end point, one must also emphasize that, in this well-documented registry, no symptomatic or asymptomatic patient of the >1000 studied followed over an overall median of 96 months actually died or had residual adverse sequelae, whereas complications related to catheter ablation included complete atrioventricular block leading to a lifetime exposure to permanent pacing and left bundle-branch block in 3 with unknown longer-term consequences—this in the hands of a very experienced high-volume center. These findings are similar to outcomes observed elsewhere,1 namely, a small incidence of VF (aborted in a majority) almost exclusively observed in the pediatric population. Because of the absence of fatalities, the registry data in reality reinforce the failure of an effort to screen and ablate patients to improve hard outcomes of preventing death.

One might pause and consider further. None died! This is a truly extraordinary statistic, that is, 15 clinical VFs without any mortality or sequelae in anyone! All 15 patients with VF (13 initially grouped as asymptomatic) experienced symptoms before VF (presyncope in 10 and dizziness in 5) allowing for medical attention. VF is not immediate in the great majority of WPW patients, and the lag time of intermediate arrhythmias results in patients coming to medical attention because of tachycardia-related symptoms. Indeed, the authors acknowledge that “patients and parents have been well educated and

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alarmed to immediately reach hospital or emergency services at beginning of symptoms. In fact, 8 patients had VF in the hospital, and many had premonitory symptoms. The registry argues for VF associated with WPW as being fundamentally dissimilar to VF associated with potentially more malignant entities (e.g., coronary disease, long QT syndrome, etc).

The majority of the WPW population indeed have an excellent prognosis, as reaffirmed by the registry data. The reported low VF incidence of 1.9 per 1000 patient-years of follow-up in the asymptomatic population is comparable to other publications, reporting SCD (a majority aborted) in asymptomatic WPW patients of 1.25 per 1000 person-years (95% confidence interval, 0.57–2.19). The pediatric population has been reported to have a SCD rate of 1.9 (95% confidence interval, 0.6–4.1) in comparison with 0.9 (95% confidence interval, 0.3–1.8) in adults per 1000 patient-years of follow-up (P = 0.07). This fortunately low overall risk has frustrated our ability to identify the truly at-risk patient accurately, which again resonated in this registry. An abbreviated SPRRI of <250 ms has been long accepted as the best predictor of VF, but the vast majority of individuals even with this characteristic (and with a short AP effective refractory period [ERP]), will not experience SCD (low positive predictive value). The study by Pappone et al indeed resonated with previous reports by reporting a positive predictive value for the AP-ERP of <230 ms at predicting VF of 42.4% and a negative predictive value of 100%. An end point that includes atrial fibrillation (>1 minute) with a SPRRI of <250 ms (classified as potential malignant arrhythmia), fails to recognize that a SPRRI of <250 ms has a poor positive predictive value for identifying the patient likely to experience VF (although without a SPRRI of <250 ms or AP-ERP of <230 ms, VF would be extraordinarily rare). All 78 patients experiencing so-called potential malignant arrhythmias also experienced symptoms, highlighting the importance of symptoms as an impetus to reevaluate treatment options and that even the truly asymptomatic patient generally presents to medical attention before VF.

The comparison of the asymptomatic group with the symptomatic group shows, as expected, the traditional predictors of VF in both groups albeit with a higher prevalence in asymptomatic individuals. In the symptomatic group, the decision of a minimally or moderately symptomatic patient NOT to undergo ablation would be informed by knowing that the ERP of the AP was long, and, hence, this group might be expected to be composed largely of patients screened by an electrophysiology study to be at low risk. This biases the multivariate analysis that did not demonstrate symptom status as an independent predictor of events. Indeed, there seems to be no rational reason why a symptomatic individual patient should have lower risk than an asymptomatic one! In addition, the large number screened (11 237 patients) in this registry and the small number ultimately included (2169) raises the possibility of selection bias.

As reported by Pappone et al, there is a low, albeit not zero, complication rate associated with AP ablation, even in high-volume experienced centers. It is probable that the incidence of complications/death associated with AP ablation is indeed variable in the community and that those complications may be underreported. Registry data of unenrolled patients compared with enrolled patients have been reported to indicate higher risk and receive poorer quality of care with subsequent poorer outcomes in the unenrolled patients. Similarly, the outcome data from those selected for reporting in this registry (2169 from >11 000 patients) arguably have the potential to misrepresent the real world. In 2 large studies reporting on >1300 adult patients, complications included venous thrombosis (1%), pulmonary embolii (0.3%–1.6%), thrombophlebitis (0.6%), infection (0.8%), and catheter-induced permanent complete atrioventricular block (0.1%). The registry also reported a 0.08% third-degree atrioventricular block, with ≥2% overall complication rate (including pneumothorax, femoral hematoma, fistula, left or right bundle-branch block, and pericardial effusion). Death has been reported in pediatric patients owing to cardiac perforation, coronary or cerebral thromboembolism, and ventricular arrhythmia. The overall incidence reported in this early large cohort of pediatric patients was 0.22%.

Current data including the present study cannot justify a broad screening program for asymptomatic WPW patients, nor can these data justify a more aggressive ablation approach in the asymptomatic WPW patient. A number of variables argue against the efficacy of a screening program, and, not surprisingly, this is further reinforced by the current registry data, including the low mortality/morbidity rate of asymptomatic WPW, the potential for harm by screening and subsequent electrophysiological testing and ablation, sensitivity and specificity of risk stratifiers (poor accuracy of SPRRI and AP-ERP), practicality, and cost-effectiveness. Ablation provided at the asymptomatic stage has not been demonstrated to produce outcomes superior to those of early treatment at the symptomatic stage (notably, all cases of VF were preceded by symptoms and all were resuscitated, allowing for radiofrequency ablation). Although ablation is overall safe and effective in high-volume centers, it is yet to be convincingly demonstrated as superior in the real world to the natural history in asymptomatic WPW patients. A low WPW prevalence in the population is also a barrier to cost-effectiveness.

As highlighted by many publications, risk factors for identifying the truly high-risk patient lack accuracy. However, the identification of factors generally associated with a favorable long-term outcome is somewhat easier. The abrupt and complete loss of preexcitation during sympathetic stimulation identifies APs that are incapable of rapid antegrade conduction, and thus at low risk of causing VF. Similarly, intermit-tent preexcitation generally suggests that rapid antegrade conduction is unlikely. Up to 31% of adults and 0% to 26% of children lose preexcitation over 5 years of follow-up, thus highlighting the importance of guideline recommendations to pursue initial noninvasive risk stratification in asymptomatic patients. Indeed, the registry data further support the observation of the longer AP-ERP in those who lose preexcitation in comparison with those who have persistent preexcitation (mean AP-ERP 300 ms versus 270 ms, P < 0.001). Noninvasive variables that identify lower-risk asymptomatic individuals, although not the focus of this article, may be underexploited and help clinical management.
Conclusion
Catheter ablation in the symptomatic patient is not relevant to the management of asymptomatic individuals with WPW, because it is fundamentally done to relieve symptoms, whereas ablation in the asymptomatic is done for preventing SCD. The notion that AP refractoriness is pivotal prognostically is well known. Ultimately, this registry verifies what others have shown, namely, a very low expected mortality, especially in adults. This does not convincingly argue for population screening or routine invasive testing with a view to ablation that arguably may cause more harm than good, especially in the real world outside of the higher-volume centers. The potential for complications from ablation make it difficult to make an unreserved recommendation for a primary electrophysiological assessment and ablation strategy in asymptomatic individuals. The current practice of fair and reasonable discussion of options/risks with the patient is verified, and a class IIA indication for ablation when the patient chooses this option remains reasonable.

Disclosures
None.

References
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