When Is a "Pathway" Not a Pathway?

Explaining Late Recurrences After Successful Ablation of Pediatric Atrioventricular Nodal Reentrant Tachycardia

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What sense would it make or what would it benefit a physician if he discovered the origin of the diseases but could not cure or alleviate them?

—Paracelsus (1493–1541)

Physician and alchemist Philippus Aureolus Theophrastus Bombastus von Hohenheim was born in Switzerland one year after Columbus set out for, and discovered, the New World. The son of a physician, he adopted the nom de plume Paracelsus on completion of his own medical doctorate to imply that he was at least the equal of past great physicians, such as Galen and Celsus, and is credited as the founder of the field of toxicology.[1] Paracelsus rejected Galen's theory of the four humours and advocated for the application of the scientific method to medicine, as well as the importance of the sciences in medical education.

See Article by Backhoff et al

Atrioventricular nodal reentrant tachycardia (AVNRT) is a common arrhythmia that may be successfully treated with catheter ablation; yet, the precise anatomic structures that constitute the reentrant circuit have remained the subject of study and discussion over several decades.[2–4] In contrast to the Paracelsian admonition above, modern electrophysiologists have learned to cure AVNRT, despite not yet fully discovering its origin.

In the current issue of *Circulation: Arrhythmia and Electrophysiology*, Backhoff et al[5] present data on the long-term outcome of catheter ablation of AVNRT in children. Their principal finding was that notwithstanding high rates of acute procedural success, a significant number of AVNRT recurrences occurred at long postprocedural intervals, up to 10 years after successful ablation. This is a novel finding that is at odds with pediatric electrophysiologists' clinical experience that most recurrences will occur within the first year after accessory pathway (AP) ablation; although true long-term follow-up studies of pediatric ablation are limited, Kolditz et al[6] reported an absence of recurrences after 6 months in a similarly sized cohort of pediatric patients of whom the majority (80%) had atrioventricular reentrant tachycardia.

This dichotomy in outcomes likely occurs for multiple related reasons. First, what electrophysiologists call the "slow pathway" has very little in common with usual APs that provide electrical continuity between atrial and ventricular myocardium. In an autopsy series of patients with Wolff–Parkinson–White syndrome, Becker et al[7] were able to histopathologically identify well-delineated bundles of working myocardium on the order of 1 mm in diameter in locations that correlated with the electrocardiographic pattern of preexcitation. In contrast, histopathology of the triangle of Koch, where most slow pathway ablations are performed, fails to demonstrate such small discrete pathways. The triangle has been measured in adult autopsy specimens to have (on average) sides of 18 to 20 mm and covers an area just >150 mm^2.[8]

While the macroreentrant circuit in atrioventricular reentrant tachycardia can be clearly shown to be dependent on individually identifiable structures (the atrioventricular (AV) node/His bundle and the AP), the circuit in AVNRT most likely results from a combination of the local anatomy[2] and the effects of tissue anisotropy,[9] where conduction characteristics are dependent on the arrival direction of a stimulus wavefront relative to myocyte alignment. When anisotropy is nonuniform, as in the transitional zone of the AV node, reentry can occur in small areas of myocardium without requiring block or delay in individual limbs of a reentrant circuit. Although a single ablation lesion may be sufficient to interrupt AP function, single ablation lesions in the triangle of Koch are not predictably able to render AVNRT noninducible. In the particular case of cryoablation of AVNRT, where a smaller area of myocardium is ablated than in radiofrequency (RF) ablation, there is evidence for dose-dependency related to catheter tip size, lesion duration, and bonus lesions,[10] suggesting that there is a critical area of ablation necessary to eliminate AVNRT, rather than a single specific location or pathway that must be targeted.

The third potential reason for late recurrences in pediatric patients arises from the observation that the anatomy of the triangle of Koch and the AV nodal inputs are subject to change with age and growth, whether measured directly at autopsy[11] or in vivo via electroanatomic mapping.[12] Not surprisingly, these anatomic changes are accompanied by age-related changes in AV nodal physiology.[13] Thus, an AVNRT ablation that renders a pediatric patient noninducible in the EP laboratory may no longer be sufficient years later, after a period of linear growth with resulting changes in the underlying electrophysiological substrate, creating additional opportunities for reentry.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Finally, electrophysiologists consider the presence or absence of a slow pathway differently from APs, and the presence or absence of a slow pathway does not reliably predict the inducibility of AVNRT. APs typically demonstrate one or more of manifest preexcitation, noncentral/nondecremental retrograde activation, and inducibility of atrioventricular reentrant tachycardia with confirmation by provocative maneuvres. In contrast, the presence of a slow pathway as part of dual AV nodal physiology (DAVNP) may be seen in almost two thirds of pediatric patients without arrhythmias.[14] Similar to adults with DAVNP, only a minority of pediatric patients with DAVNP will have inducible AVNRT. However, the converse discrepancy also exists—only about half of pediatric patients with AVNRT will demonstrate classical DAVNP, while the alternate (and sometimes complementary) finding of sustained slow pathway conduction is only slightly more common.[15,16]

Further, as seen in the current study, after successful ablation where AVNRT is no longer inducible, there may be evidence of residual slow pathway function (often referred to as modification or modulation of the slow pathway), which does not predict recurrence of AVNRT after RF ablation; in one study[17] of transesophageal electrophysiology studies performed an average of 3 years after successful RF ablation of AVNRT, this residual form of DAVNP was shown to be persistent but did not predict AVNRT recurrence. There is divergent evidence[10] on whether residual slow pathway function is a predictor for recurrence after cryoablation; the smaller lesion area associated with cryoablation may explain this difference between RF and cryoablation. In the current study (Figure 1C and 1D), there was no statistical difference between the Kaplan–Meier curves for either RF or cryoablation, but there was a qualitative appearance of divergence in the curves between cryoablation and cryomodification; as the authors note, the study was not sufficiently powered to evaluate this outcome.

Going forward, the difficulty in determining the location of the slow pathway in children with AVNRT may be partially addressed through the search for slow pathway potentials, either directly by electrogram or through the use of electroanatomic mapping tools.[18,19] Larger studies[20] of AVNRT ablation in children will assist pediatric electrophysiologists in achieving long-term success, while at the same time limiting or eliminating complications. In young patients, clarity of end points is important to protect against additional ablation lesions that may increase the risk of AV block (seen in 1.8% of patients in the current study) without improving long-term outcomes.

Whether wine is a nourishment, medicine or poison is a matter of dosage

—Paracelsus

Disclosures

None.

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