Editorial

Could predicted post-pacing interval from theoretical mathematical formula replace the observed post-pacing interval in clinical practice?

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Waldo and colleagues originally described entrainment in 1977 (1). The proposed criteria for the recognition of entrainment were proposed: (I) when pacing at a constant rate that is faster than the rate of the tachycardia and which fails to interrupt it, constant fusion beats in the electrocardiography (ECG) are demonstrated during pacing except for the last captured beat, which is not fused; (II) during a tachycardia, when pacing at two or more constant rates that are faster than the rate of the tachycardia but fails to interrupt it, there is the demonstration of constant fusion beats in the ECG at each rate, but different degrees of constant fusion at each rate (2,3); (III) during a tachycardia, when pacing at a constant rate that is faster than the rate of tachycardia and which interrupts it, there is the demonstration of localized conduction block to a site or sites for one beat followed by activation of that site or those sites by the next paced beat from a different direction are demonstrated and associated with a shorter conduction time (3); (IV) during a tachycardia, when pacing at two constant rates that are faster than the rate of tachycardia, but which fail to interrupt it, there is the demonstration of a change in conduction time to and electrogram morphology at an electrode recording site (4).

Over four decades, this principle was used as a main tool for an intellectual understanding of reentry, differentiation of various supraventricular tachycardias, and was utilized in basic strategies for localization of critical areas for ablative therapies. Various empirically-derived diagnostic entrainment criteria were established for tachycardia differentiation (5-9). Recently, attention has shifted toward catheter ablation of ventricular tachycardia. Studies by Stevenson *et al*. divided reentry circuits into one or more functional components, which helped conceptualize the reentry circuit and predict the likelihood that ablation could terminate ventricular tachycardia (10). Although the benefit and advantage of entrainment are confirmed, interruption of tachycardia during entrainment is not uncommon. Maneuvers that were used, including pre-excitation index and his refractory premature ventricular complex, use interrupted tachycardia circuit without calculating for the post-pacing interval (PPI) to differentiate the mechanism of supraventricular tachycardia. Could the timing of entrainment interruption be used for diagnostic purposes, even with termination of the tachycardia?

In this issue of the Journal, Daniel W. Kaiser and colleagues described and provided proof of the concept of their study, which investigated the relationship between the number needed to entrain (NNE), the tachycardia cycle length (TCL), the overdrive pacing cycle length (PCL), and the PPI on the timing of tachycardia entertainment (11). In the first part of the study, they derived the equations: $NNE=|(PPI-TCL)/(TCL-PCL)|+1$ and [$Advancement= (NNE-1) * (TCL-PCL)–(PPI-TCL)$], which are determined by regularly measured intracardiac parameters from two typical atrial flutter patients. In the second part of the study, they validated the high correlation between the PPI-TCL and the predicted PPI-TCL (calculated as [$(NNE-1) * (TCL-PCL)$ – tachycardia advancement]). Their result theoretically unifies the various seemingly disparate methods of differential diagnosis in supraventricular and ventricular tachycardia. The study offers an alternative diagnostic tool in reentry arrhythmia. This study is noteworthy for several reasons.

First, it unifies various relationship observed in many previous studies or textbooks using entrainment maneuvers for diagnostic purposes, including observed PPI-TCL, pre-excitation index, the summed pre-excitation index, the entrainment index, and the behavior of atrial electrograms in the transition zone. All the entrainment maneuvers showed the similar result: the longer distance from the circuit, the longer the PPI-TCL, and more prematurity needed for resetting the tachycardia. Second, the analysis of observed PPI has significant limitations, which could be overcome by predicted PPI-TCL with less overdrive beats: (I) decremental conduction inside or outside the circuit; (II) difficulties in measuring signals at the pacing site; (III) delay between stimulus and local electrogram; (IV) difficulties in identifying the highly fractionated electrogram components, which was captured by overdrive pacing. Predicted PPI-TCL provides an alternative choice instead of entrainment. Third, the application of the concept is useful when the right ventricular (RV) overdrive pacing frequently terminates tachycardia in diagnostic electrophysiological study. Fourth, the result could be applied on the anti-tachycardia pacing (ATP) algorithms by recording the PPI of a failed ATP attempt. In case of left ventricular tachycardia with PPI-TCL as long as 180 ms (the longest value in present study), PCL with 10 ms shorter than TCL required more than 18 beats to entrain the VT circuits (according to equation by Daniel W. Kaiser *et al.*). However, traditional ATP tries three attempts of 8-beat ATP drive, which would fail in cases with very long PPI-TCL. Auto resetting of programmed ATP based on previous failed ATP attempt provides a better efficacy in the ATP therapy.

There are several aspects that warrant emphasis in this study. First, although several limitations exist in the analysis of PPI, it is easier to obtain PPI directly than calculated the predicted PPI-TCL in clinical practice. The calculation of predicted PPI-TCL takes more time than direct measurement of the PPI-TCL in clinical electrophysiological study.

Second, the patient selection for this concept is important. Abnormal conduction properties resulting from prior scar or extensive ablation could interfere with the analysis. Overdrive pacing may alter the conduction velocities and repolarization properties of the intervening tissues or critical pathways involved in reentry, especially in ventricular tachycardia. Ventricular electrograms, which displayed decremental conduction, are likely to participate in reentrant ventricular tachycardia circuits (12). Besides, the reentry circuits of ventricular tachycardia can be large and complex. QRS morphology during tachycardia and overdrive pacing, PPI-TCL, S-QRS interval were important parameters to divide reentry circuit into functional components, including proximal isthmus, central isthmus, exit, entrance, inner loop, outer loop, and remote bystander (10). The proposed concepts in this study help to interpret and guide entertainment maneuvers, while realizing clinical electrophysiology may not always behave exactly according to the mathematical theories.

Third, the mathematical theories are imperfect reflection of clinical practice. The authors provided good correlation between observed PPI-TCL and predicted PPI-TCL by Spearman rank test in the second part of the study. If the authors wanted to use the predicted PPI-TCL to replace the observed PPI-TCL with previous published cut-off value, intraclass correlation coefficient might provide more information instead of Spearman rank test. However, the clinical benefit of diagnostic value of predicted PPI-TCL was not compared with traditional one. In this study, the predicted PPI-TCL value was smaller than observed PPI-TCL in spite of various tachycardias. Adjustment of predicted PPI-TCL to meet the established criteria was not provided.

Forth, the design of this study was not straightforward. The main purpose of this study was to investigate the relationship among the n, TCL, PCL, and PPI. Authors selected two patients with typical atrial flutter for proof of concept in their hypothesis. This population was chosen because the reentrant circuit of typical atrial flutter is anatomically well-defined and less susceptible to decremental conduction. For validating the mathematical formula, it might be more convincing to perform in supraventricular and ventricular tachycardia separately. I believed different degree of bias might exist between supraventricular and ventricular tachycardia. Beside, the locations of ventricular tachycardia circuits and type of cardiomyopathies were not mentioned in this study. The PPI-TCL from RV apex catheter ranged from 20 to 180 ms in this study. That means the ventricular tachycardia circuits in this study included RV circuit or bundle branch reentry ventricular tachycardia and LV circuits.

Many questions remained unanswered in this study. Could predicted PPI-TCL replace observed PPI-TCL in typical flutter, atrioventricular nodal reentry tachycardia, atrioventricular reciprocating tachycardia, and ventricular tachycardia? Should traditional cut-off value of PPI-TCL

(±30 ms) change in predicted PPI-TCL? Could predicted PPI-TCL provide the same diagnostic power as observed PPI-TCL? What kind of reentry tachycardia is suitable for this formula? It is hoped that some of these critical questions will be answered by the further studies with predicted PPI-TCL versus observed PPI-TCL for diagnosis of different kinds of reentry tachycardia. Physicians considering this mathematical formula for clinical interpretation should wait for more data from well-designed validation studies and head-to-head comparison to establish its utility as a diagnostic tool.

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Footnote

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