Changes in Atrioventricular Node Physiology Following Slow Pathway Modification in Patients with AV Nodal Re-entrant Tachycardia: The Hypothetical Suggestion of Mechanism of Noninducibility of AVNRT

Ju Youn Kim, MD; Sung-Hwan Kim, MD; Tae-Seok Kim, MD; Ji-Hoon Kim MD, PhD; Sung Won Jang, MD; Yong Seog Oh, MD, PhD; Seung Won Jin, MD, PhD; Tai Ho Rho, MD, PhD; Man Young Lee, MD, PhD

Division of Cardiology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

ABSTRACT

Background and Objectives: In cases of radiofrequency catheter ablation (RFCA) for patients with atrioventricular nodal re-entrant tachycardia (AVNRT), complete elimination of slow pathway is not always achievable. Furthermore, in situations of the so-called modified slow pathway, the underlying mechanism of tachycardia elimination remains unclear.

Subjects and Methods: Patients who underwent RFCA for AVNRT, and showed persistence of dual atrioventricular nodal physiology but no induction of AVNRT after ablation were enrolled. We measured electrophysiologic parameters before and after the ablation procedure.

Results: The study subjects included 31 patients (39% men; mean age 43±19 years). The RR interval, Wenckebach cycle length of AV node, slow pathway effective refractory period, maximal AH interval of fast pathway and slow pathway showed no significant changes before and after ablation. However, fast pathway effective refractory period (360±67 vs. 304±55, $p<0.001$) and differences between slow pathway effective refractory period and fast pathway effective refractory period (90±49 vs. 66±35, $p=0.009$) were decreased after slow pathway ablation.

Conclusion: We suggest a possible relationship between the mechanism of tachycardia elimination in AVNRT and an alteration of the re-entrant circuit by removal of the atrial tissue in Koch's triangle. This may be a critical component of providing the excitable gap for the maintenance of tachycardia rather than the electrical damage of slow pathway itself.

Key Words: ▪Atrioventricular Nodal Re-entrant Tachycardia ▪Slow Pathway ▪Catheter Ablation

Introduction

Radiofrequency catheter ablation (RFCA) of the slow atrioventricular (AV) nodal pathway, guided by anatomic landmarks or targeting the slow pathway potential from intracardiac electrograms, has become the treatment of choice in symptomatic patients with AV nodal re-entrant tachycardia (AVNRT).[1] Based on the favorable clinical results, regardless of the presence of slow pathway following ablation, both the elimination of slow pathway conduction or persistence of dual AV node physiology without induction of AVNRT have been regarded as a successful RFCA end point of AVNRT. Thus, the elimination of the slow pathway conduction is not required, in terms of a cure, for AVNRT with ablation.[2-6] However, the mechanism of noninducibility of AVNRT despite the remaining slow pathway is still unclear.

To understand the mechanism of this noninducibility, we assessed changes in the electrophysiologic properties of the AV node after RFCA.

Subjects and Methods

Patients

The study subjects were 31 consecutive patients (39% men; mean age, 49±19 years) with typical AVNRT, who underwent slow pathway ablation. All patients had documented AVNRT by electrocardiogram. Antiarrhythmic drugs were withheld at least five half-lives before the electrophysiologic procedure. All of the induced AVNRT were slow/fast form of AVNRT. The dual AV node physiology was noted before ablation and persisted even after successful ablation procedure.

Electrophysiologic study

Each patient received an informed written consent form detailing the electrophysiologic study and ablation procedure. We used a total of four electrode catheters and the following catheter positions. Two quadripolar electrode catheters with 5 mm spacing (Daig Corp., St. Jude Medical Inc., Minnetonka, MN, USA) introduced via the left femoral vein and positioned at the high

right atrium and right ventricular apex. A hexapolar catheter with 2-5-2 mm spacing (Response™, Daig Corp., St Jude Medical Inc.) positioned at the His bundle site. A decapolar catheter with 2-8-2 mm spacing inserted into the left subclavian vein and positioned in the coronary sinus (Daig Corp., St Jude Medical Inc.).

Then, induction of AVNRT was performed by electrical stimulation. Bloom Stimulator (Fisher medical technologies, Bloomfield, CO, USA) was used for the test, and intracardiac electrograms were filtered with band-pass of 30-500 Hz and amplified (2,500-10,000 times) using Prucka Cardio Lab 7000 system (G.E. Medical systems, Milwaukee, WI, USA). Programmed stimulation from the high right atrium and right ventricular apex were performed. Incremental pacing or programmed stimulation using up to two extra stimuli testing were applied.

We measured the electrophysiologic parameters before and after the ablation procedure. We measured the heart rate, AV node Wenckebach cycle length (AVN-WCL), effective refractory period (ERP) of the fast and slow pathways and their difference, and the maximal atrio-His interval of the fast and slow pathways (Figure 1). Dual AV node physiology was defined as a 50 msec increase of the S2-H2 interval in response to a 10 msec decrease in the S1-S2 coupling interval with atrial extra stimulus testing. In order to minimize the pharmacologic influence on autonomic changes, we performed post-ablation evaluation at least 30 minutes after the discontinuation of isoproterenol infusion, and the heart rate returned to baseline rate.

RF current was delivered to the region between the orifice of the coronary sinus and the tricuspid annulus guided by an electrographic and a fluoroscopic view. Application of energy was interrupted if junctional beats did not appear within 10 seconds of RF energy delivery or if impedance increased abruptly. The RF current was delivered up to 50 watts and limited by temperature <60°C. Once junctional beats appeared, we applied the RF current for 60 seconds. Successful ablation was defined as noninducibility of AVNRT and the absence of two or more consecutive AV nodal echoes. We administered isoproterenol if it had been necessary for induction before ablation. We confirmed noninducibility 30 minutes after the last RF current.

All patients were followed up for at least 1 year, and no recurrence was observed.
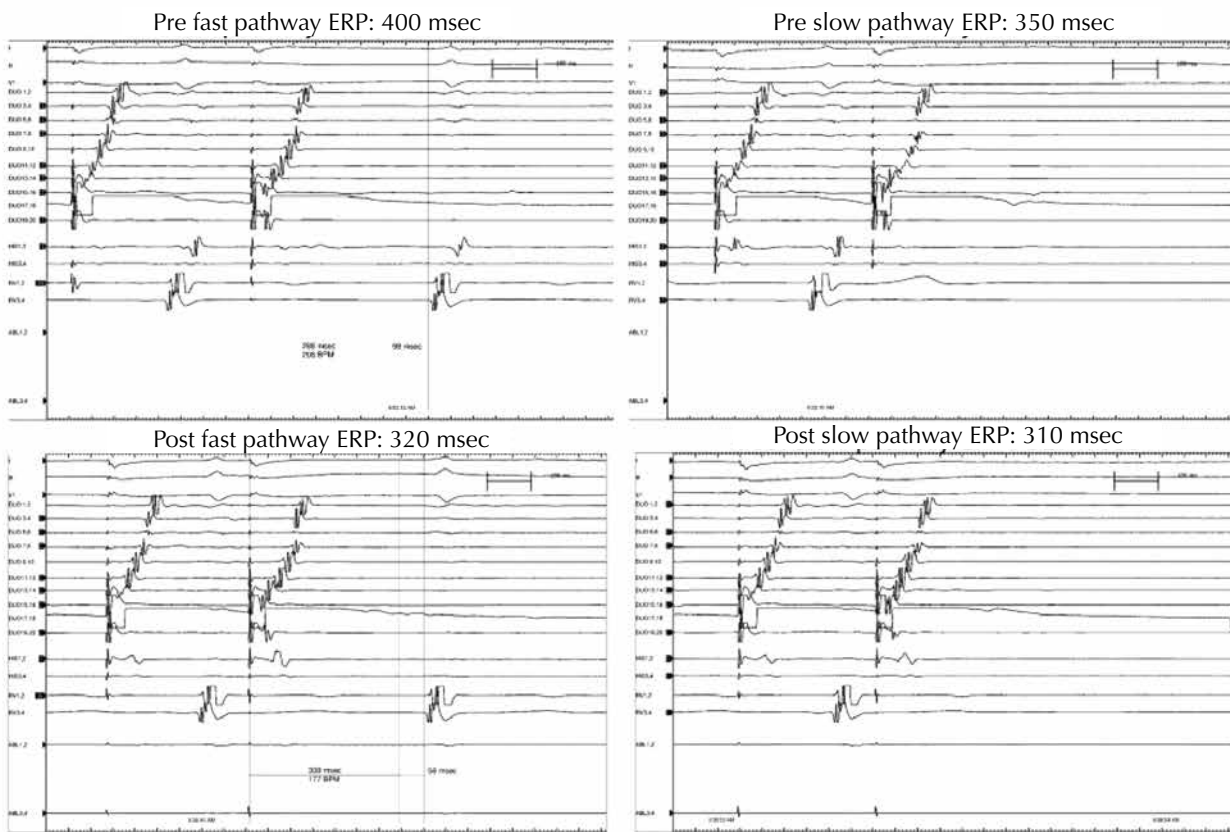
Figure 1. Representative case of measurement of AV node parameters. The ERP of the fast pathway, defined as the longest premature coupling interval that results in failure of conduction by the fast pathway, presented with an AH jump. The ERP of the slow pathway, defined as the longest A-A interval that fails to propagate to the His bundle after the AH jump.
AH, Atrio-His; AV, atrioventricular; ERP, effective refractory period.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows 12.0. Continuous data were expressed as the mean±SD and were compared using two-tailed paired Student's t-test. P values <0.05 were regarded as statistically significant.

Results

Patients

Based on the end point of noninducibility of AVNRT, RF ablation was successful in all 31 patients. The mean age was 43±19 years, and 39% of the patients were men. All patients had dual AV node physiology, and the typical AVNRT was inducible. None of the patients experienced AV node injury to show transient or persistent AH prolongation after delivery of RF energy.

AV node parameters

The electrophysiologic parameters before and after ablation are summarized in Table 1. RF ablation did not lead to significant modification of the electrophysiologic properties of slow pathway. Baseline sinus RR interval was 797±142 msec and AVN-WCL was 379±60 msec. No significant changes were found in the RR interval (p=0.065) or cycle length that induce Wenckebach periodicity in the AV node (p=0.300) before and after RF

Table 1. Electrophysiologic parameters before and after RFCA

Electrophysiologic Parameters (msec)	Before RFCA	After RFCA	P
RR interval	797±142	761±139	0.065
AVN-WCL	379±60	368±47	0.300
Fast pathway ERP	360±67	304±55	<0.001
Slow pathway ERP	263±50	242±47	0.063
SP_{ERP}-FP_{ERP}	90±49	66±35	0.009
Maximal AH interval of FP	181±54	190±53	0.329
Maximal AH interval of SP	348±100	362±138	0.606
Maximal AH SP-FP	170±89	156±102	0.512

AH, Atrio-His; AVN-WCL, atrioventricular node Wenckebach cycle length; ERP, effective refractory period; FP, fast pathway; RFCA, radiofrequency catheter ablation; SP, slow pathway.

ablation. Baseline ERP of the fast pathway was 360±67 msec, which was shortened after the procedure (304±55 msec, $p<0.001$).

However, the ERP of the slow pathway showed no significant change before and after ablation ($p=0.063$). The differences between ERP of the fast and slow pathways significantly decreased ($p=0.009$). Maximal AH interval of the fast ($p=0.329$) and slow pathway ($p=0.606$) and the differences ($p=0.512$) between them did not change significantly.

Discussion

RFCA has achieved a status of curable treatment modality for AVNRT,[7,8] and the elimination of slow pathway conduction is considered the standard treatment of AVNRT. However, it is accepted that the complete elimination of slow pathway conduction is not an absolute requirement for a favorable clinical outcome.[2,4,6] Slow pathway conduction remains to be observed in 24% to 68% of cases even after successful ablation of AVNRT,[2-6] in which of so-called slow pathway modification. This is an interesting phenomenon because an apparent failure of eliminating the actual target of ablation could result in a cessation of tachycardia. Several studies exploring the electrical change of slow pathway, suggest noninducibility of AVNRT despite the persistence of a slow pathway after RF ablation.

Previous studies of the changes in AV node physiology

As a summary of the previous studies, ablation of the SP could result in a variable degree of changes as shown in Table 2. Similar to our study, Lindsay et al.[9] reported a decrease in the fast pathway ERP with no changes in other parameters including slow pathway ERP and maximal AH interval of the slow and fast pathway. Haissaguerre et al.[10] reported that the maximal AH interval of the slow pathway decreased, and the differences between other parameters showed no significant changes. In this study, we included all patients with both complete elimination and modification of the slow pathway. Lastly, Posan et al.[11] have shown that slow pathway ERP increased after SP ablation, resulting in the decrease of differences between the ERP of the fast and slow pathways; similar to our results.

Possible mechanisms of nonindicibility of AVNRT after slow pathway modifications

Although an inconsistent change in AV node physiology after the modified slow pathway was found, several mechanisms are proposed to explain this nonindicibility. First, the slow pathway itself may be partially injured and rendered unable to sustain tachycardia.[5] Second, the ablation may eliminate the culprit slow pathway and reveal another "non-arrhythmogenic" pathway that did not course through the region between the tricuspid annulus and the coronary sinus ostium.[12] Lastly, the interaction between the slow pathway and the fast pathway may have changed to prevent tachycardia.[13]

Posan et al.[11] reported a decrease in the AH interval of the slow pathway after ablation and suggested a mechanism of a remnant single echo beat. The paradoxically-enhanced slow pathway conduction combined with the shortening of ERP of the retrograde fast pathway after ablation[14,15] resulted in a single echo. In the present study, the maximal AH interval, ERP, and Wenckebach cycle length of the slow pathway did not show significant differences between pre- and post-ablation. As shown in Table 2, the electrophysiologic changes of the slow pathway after RFCA[5] were variable. Furthermore, the degree of those changes seemed to be mostly insignificant and not consistent.[3,9,16] Considering the results of previous studies, the concept of a simply injured slow pathway seems to be the lack of a rationale to explain the noninducibility.

A second hypothesis is based on an anatomic observation. Inoue et al.[17] analyzed the inferior AV nodal extensions in human autopsies and proposed their involvement as the anatomic substrate of the slow pathway. The inferior AV nodal tissue extended rightward and leftward, or toward both. Thus, ablation from the right side of the septum could eliminate only a rightward extension and leave the leftward extension. However, when we investigated why the remaining leftward extension of the AV nodal tissue could not carry the role as a slow pathway to induce the AVNRT, it does not seem to be plausible and neither applicable to all patients. In our series of patients, successful results were all achievable by ablation confined to the right side of the septum. In addition, it is unlikely that the non-clinical pathway that emerged after ablation shares the similar electrophysiologic characteristics with the originally targeted slow pathway.

The third explanation is the change of interaction between the slow and fast pathways. The slow and fast pathways must have proximal and distal continuities to complete the re-entry circuit whether perinodal tissues are involved or not. However, the anatomic basis and functional properties of these continuities have not yet been confirmed. In addition, whether the re-entrant circuit is purely intranodal or contains extranodal atrial inputs is not clearly defined.

There are evidences of atrial tissue participation in the slow/fast form of AVNRT.[7,12] One of which is a rare occurrence of a block

Table 2. Changes in AV node physiology after SP ablation

	Present study	Haissaguerre et al.	Lindsay et al.	Takahashi et al.	Posan et al.
Fast pathway ERP	↓	-	↓	-	-
Slow pathway ERP	-	-	-	- / ↑	↑
SP$_{ERP}$-FP$_{ERP}$	↓	-	↓		↓
Maximal AH interval of FP	-		-	-	
Maximal AH interval of SP	-	↓	-	- / ↑	↓
Maximal AH SP-FP	-		-		

↓, decrease; ↑, increase; -, no change; AH, Atrio-His; ERP, effective refractory period; FP, fast pathway; SP, slow pathway.

to the atrium during tachycardia. Studies using optical mapping techniques have established the involvement of the perinodal atrial tissue and transitional cells in the re-entry circuit.[18] Furthermore, in terms of tissue change after catheter ablation, the actual amount of RF injury to the transitional cells, the degree of injury to the compact node, and the effect of the uncoupling of the superficial atrial fibers from the subjacent compact nodal transitional cells are not pathologically understood[19]; the AV node was morphologically and histologically normal after RF ablation.[20]

Our study results apply to the third hypothesis suggesting the disruption of interaction mediated by perinodal atrial tissue between the slow and fast pathways. We could not find any significant electrophysiologic changes in slow pathway after slow pathway modification. However, this explanation is too simple to clarify the role of perinodal atrial tissue in the re-entrant path of AVNRT. Herein, to support the disruption of interaction mediated by perinodal atrial tissue between the slow and fast pathways as a principal mechanism of noninducibility, we would like to propose the hypothesis based on the wavelength hypothesis. The AVNRT circuit is classically suggested to be confined within Koch's triangle surrounded by the tendon of Todaro, the coronary sinus ostium, and the tricuspid annulus. When reentry begins, these anatomical structures could behave functionally as electrical conduction barriers, such as crista terminalis, in a case of classical atrial flutter[21] and sustain AV nodal reentry within a limited space of Koch's triangle. In clinical practice of RF ablation on the AVNRT, the approach guided by anatomic land mark is commonly used, presuming the location of the slow pathway is between the tricuspid annulus and the anterior tip of the coronary sinus ostium. A series of ablations, even though the number of RF energy applications vary, are usually delivered from the posteroseptal area toward the midseptum along the annulus of the tricuspid valve. This series of RF lesions could result in the loss of the atrial tissue inside Koch's triangle. This removal of atrial tissue, regardless of its role in the re-entrant path of the AVNRT inside Koch's triangle, could make the nodal re-entrant circuit confront the loss of spatial room that might be necessary for its free rotation. According to the wavelength hypothesis, the re-entrant path should be able to accommodate the wavelength itself by providing the excitable gap either functionally or anatomically. In other words, repeated

ablations inside Koch's triangle hamper this area to hold the re-entrant circuit of AVNRT, such as the compartmentalization of atrial tissue, in a maze operation for atrial fibrillation. The loss of the atrial tissue involved providing the excitable gap for the reentry of AVNRT could result in suppression of re-entrant tachycardia (Figure 2). Our explanation applies to the mechanism of noninducibility of AVNRT showing the persistence of slow pathway in patients who have RF ablation of the so-called slow pathway modification for AVNRT.

Limitation

We based our explanation on the wavelength hypothesis. This concept assumes that the re-entrant path of AVNRT is a two-dimensional structure and the tendon of Todaro functions as an electrical barrier such as the crista terminalis or the Eustachian ridge in the classical atrial flutter. However, these findings are not supported by solid electrophysiological evidence. Second, we cannot assure that current electrophysiologic measurements are truly relevant to the actual electrical changes of the damaged slow pathway, but we have to admit that no other comparable and
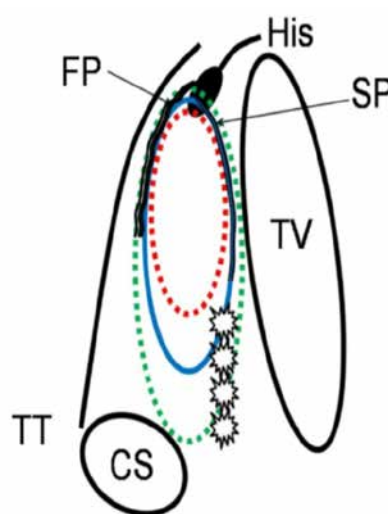

Figure 2. Diagram showing the mechanism of noninducibility of AVNRT despite the persistence of dual AV node physiology. Assuming the AVNRT wavelength as the blue circle, the anatomic re-entrant path (green, dotted line) is able to incorporate the AVNRT wavelength (blue circle) before ablation. However, as a result of the repeated ablations delivered on posterior and mid-septal areas, the anatomical re-entrant path has shrunk (red, dotted line), and cannot accommodate the original AVNRT wavelength.
CS, coronary sinus; FP, fast pathway; SP, slow pathway; TT, tendon of Todaro; TV, tricuspid valve.

practical methods are available to replace this measurement in clinical practice. Third, isoproterenol was administered in some cases for induction of AVNRT. The electrophysiologic parameters were measured before the isoproterenol infusion. Although post-ablation measurement was performed at least 30 minutes after the stop of isoproterenol infusion, it could influence to autonomic functions.

Conclusion

We could not find any significant electrophysiologic changes in the slow pathway from the so-called SP "modification." We suggest that the mechanism of tachycardia elimination in AVNRT is related to an alteration of the re-entrant circuit by removal of the atrial tissue in Koch's triangle, which may be a critical component likely to provide the excitable gap for the maintenance of tachycardia rather than the electrical damage of the slow pathway itself.

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