Effective Refractory Periods in the Right Atrium in Patients with Atrioventricular Nodal Reentrant Tachycardia

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TOKANO ET AL.: ***Effective Refractory Periods in the Right Atrium in Patients with Atrioventricular Nodal Reentrant Tachycardia*****. Introduction:** Atrial flutter and fibrillation (AFL/AF) are frequently induced in patients with atrioventricular nodal reentrant tachycardia (AVNRT), however, its mechanism is uncertain. The purpose of this study was to determine characteristics of effective refractory periods in the right atrium (RA) in patients with AVNRT. **Methods and Results:** In 26 patients with typical AVNRT (21 female, mean 46-year-old), AFL/AF was induced in 9 (35%) patients during an electrophysiologic study before slow pathway (SP) ablation. The atrial effective refractory periods (A-ERP) were measured at the high, mid and low lateral wall in the RA, the high and mid RA septum, and the SP region. Dispersion in the A-ERP (the longest – shortest; ERPD) was also calculated. The data was compared with 28 patients with intra- or infra-nodal atrioventricular block (AVB) and 32 patients with sinus node dysfunction (SND). The mean A-ERP was from 196 to 220 msec excepting at the SP region. The A-ERP at the SP region was significantly longer comparing with those at the other sites (mean 242 msec, $p<0.05$). Similar tendency was found in patients with SND, not in patients with AVB. The ERPD was significantly greater than that in patients with AVB (mean 72 versus 45 msec, respectively, $p<0.05$) while it was similar to that in patients with SND (mean 78 msec). **Conclusion:** In patients with AVNRT, the A-ERP in the SP region was relatively prolonged and the ERPD was wide as in patients with SND. These atrial electrophysiologic abnormalities might be potentially arrythmogenesis for atrial tachyarrythmias other than AVNRT. *(J HK Coll Cardiol 2012;20:31-37)*

Atrioventricular nodal reentrant tachycardia, Atrial flutter, Atrial fibrillation, Refractory periods

摘要

引言：房室結折返性心動過速常常誘發房撲、房顫，然而，其形成機制尚不清楚。本研究的目的在於測定房室折返性心動過速患者右心房有效不應期的特徵。**方法和結果：**在26例典型的房室結折返性心動過速患者（21位女性，平均年齡46歲）中，有9例病人（35%）在慢徑消融的電生理學研究中發生房顫。在右心房側壁高、中、低位，右房間隔高、中位及慢徑路區測定有效不應期；並計算心房有效不應期的離散度（最長—最短；有效不應期空間離散度）。將所測得的資料分別與28例房室結下房室傳導阻滯患者和32例竇房結功能障礙患者的資料進行比較。除慢徑路區外，右心房平均有效不應期爲196-220 msec；而慢徑路區的有效不應期明顯長於其他部位（平均242msec，$p<0.05$）。在竇房結功能障礙的患者中也發現了相似的趨勢，而房室傳導阻滯的患者中則無。此外，右心房有效不應期的空間離散度明顯大於房室傳導阻滯的患者（平均72 msec對45 msec，$p<0.05$），而與竇房結功能障礙的患者相似（平均78 msec）。**結論：**在房室結折返性心動過速的患者中，慢徑路區右心房有效不應期相對性延長，有效不應期空間離散度大，這與竇房結功能障礙的患者相似。這些心房電生理異常可能是潛在的致房性心律失常的因素而非房室結折返性心動過速。

關鍵詞：房室結折返性心動過速，房撲，房顫，不應期

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Introduction

Atrioventricular nodal reentrant tachycardia (AVNRT) is a common supraventricular tachyarrhythmia in the clinical setting. An electrophysiologic study (EPS) is performed for its diagnosis, usually before slow pathway (SP) ablation. Previous studies have reported that atrial flutter and/or fibrillation (AFL/AF) are frequently complicated and induced during the EPS in patients with AVNRT.[1-8] However, the details of AFL/AF coexistence with AVNRT is still not clear.

The purpose of this study is to determine electrophysiologic characteristics of the right atrium (RA), especially effective refractory periods and its dispersion, in patients with AVNRT.

Methods

The study subjects were 26 patients with a typical (slow-fast form) AVNRT and structurally normal heart in whom an EPS and subsequent SP ablation were performed. Twenty-one patients were female and remaining 5 patients were male. The age was 46.1±14.9 (range 21-76) year-old. All patients did not have a natural history of AFL/AF. The patients with underlying cardiovascular disease such as coronary artery disease, cardiomyopathy, valvular heart disease, hypertension and the other kind of arrhythmias were not included in this study subject. Therefore, patients who showed abnormal findings on the chest X-rays, baseline 12 leads electrocardiogram and echocardiogram were excluded in this study.

The baseline EPS was performed using standard techniques at unsedated fashion. Briefly, quadpolar electrodes catheters were placed at the high RA, His bundle region and the right ventricular apex. A decapolar electrodes catheter was placed in the coronary sinus. To minimize the effect of pacing on the atrial refractoriness, atrial effective refractory periods (A-ERP) in the six different sites in the RA were measured using the atrial extra-stimuli at a basic cycle length of 600 msec with 10 msec gradual decrement moving a quadpolar electrodes catheter at high, mid and low lateral wall in the RA, high and mid RA septum, and low RA septum (SP region). If an AVNRT was induced, it was immediately terminated with an atrial or ventricular burst pacing as soon as possible. Then, routine study included an atrial burst pacing up to a rate of 200 pacing per minute, sinus node overdrive suppression test, a ventricular burst pacing and ventricular extra-stimuli were performed. Inducibility of AFL/AF in the EPS that lasted over 10 seconds was also noted. We defined the dispersion in A-ERP (ERPD) as the difference in the longest and shortest A-ERP among the six sites in the RA. If AVNRT was not induced, subsequent provocative EPS was performed. However, the all A-ERP data was obtained before the routine baseline EPS.

The ERPD was compared with those in 28 patients with intra- and infra-Hisian atrioventricular block (AVB) without episodes of any atrial tachyarrhythmias (age: 76.8±10.5 year-old, 11 male) and 32 patients with sinus node dysfunction (SND) (age: 77.0±10.4 year-old, 15 male). In the group of SND, AFL/AF were clinically documented before the EPS in 15 patients (47%). In contrast, patients who had a history of AFL/AF were not included in the group of AVB. In these patients group, coronary sinus catheter was not placed, however, A-ERPs in the RA and ERPD were obtained using same technique in patients with AVNRT. Inclusions for these patients group were indicated in Table 1.

All patients were provided written consent to this study approved by the institutional research ethics committee.

Results

All patients showed a dual atrioventricular nodal physiology and induced a typical AVNRT by using the atrial burst pacing and/or extra-stimuli during the EPS. No patients showed findings that indicated SND and abnormal atrioventricular and intraventricular conduction.

AFL/AF was induced in 9 (35%) patients. AFL was induced in 3 patients, and AF was induced in 3 patients. In the remaining 3 patients, both AFL and AF were induced. The intracardiac electrocardiogram indicated that the earliest activation site at the

onset of the induced AFL/AF was in the RA in all these 9 patients. The induced AFL/AF was not sustained excepting for AFL in 1 patient, however, this sustained AFL also spontaneously terminated within 1 minute. A typical case was shown in Figure 1.

The A-ERP at the six sites in the RA in patients with AVNRT were showed in Figure 2, and those in all patient groups were shown in Figure 3. As shown in Figures 2 and 3, the A-ERP at the SP region was significantly longer comparing with those at the other sites in the RA in patents with AVNRT ($p<0.05$). The ERPD was calculated as 72.3±28.0 msec in the study subjects (Figure 2). It was similar to that in patients with SND, and there was a significant difference in the ERPD between patients with AVNRT and AVB ($p<0.05$, Figure 4).

Table 1. Inclusions for compared group of patients with sinus node dysfunction (SND) and atrioventricular block (AVB)

Heart rate >60/min for patients with SND and >40/min AVB even if escape rhythm
Hemodymamically stable, no complication of heart failure
No continuous pacing is required
No marked atrial enlargement such as atrial diameter >45 mm
For patients with chronic AVB;
No history of atrial tachyarrhythmia
The study performed within 4 weeks from the occurrence of chronic AVB
The site of AVB was within or below the His-bundle

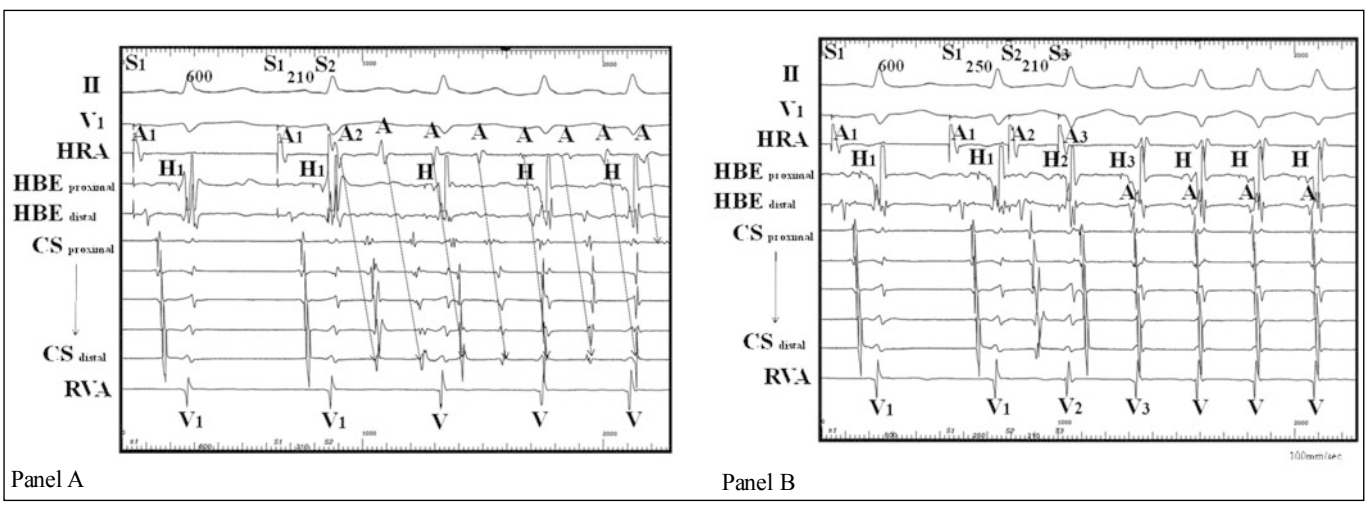

Figure 1. ***Intracardiac electrocardiogram in a typical case in which atrial flutter was induced.***
This case was a 49 year-old male with a narrow QRS tachycardia in whom atrial flutter and fibrillation had not been documented. During an electrophysiologic study, transient atrial flutter that lasted approximately 10 seconds was induced by an atrial extra stimuli (basic cycle length: 600 msec, S1-S2: 210 msec, panel A). The clinical tachycardia was induced by a double atrial extra stimuli (basic cycle length: 500 msec, S1-S2: 250 msec, S2-S3: 210 msec) under isoproterenol infusion that compatible with a typical atrioventricular reentrant tachycardia (panel B).
II, V1: surface electrocardiogram, HRA: high right atrium, HBE: His bundle electrogram, CS: coronary sinus, RVA: right ventricular apex, S: electrical stimulation, A: atrial activity, H: His-bundle activity, V: ventricular activity.

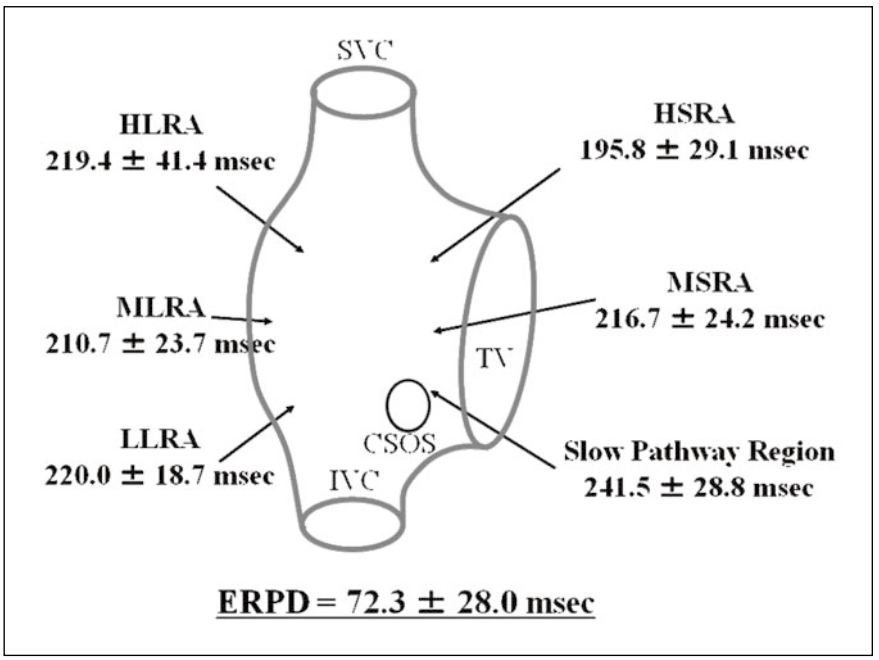

Figure 2. ***The effective refractory periods at the six sites in the right atrium in 26 patients with atrioventricular nodal reentrant tachycardia.***
The atrial effective refractory periods at the slow pathway region was significantly longer comparing with those at the other sites in the right atrium (RA) ($p<0.05$). The dispersion in effective refractory periods (ERPD) was calculated as 72.3±28.0 msec.
HLRA: high lateral RA, MLRA: mid lateral RA, LLRA: low lateral RA, HSRA: high septal RA, MSRA: mid septal RA, CSOS: coronary sinus ostium, SVC: superior vena cava, IVC: inferior vena cava, TV: tricuspid valve.

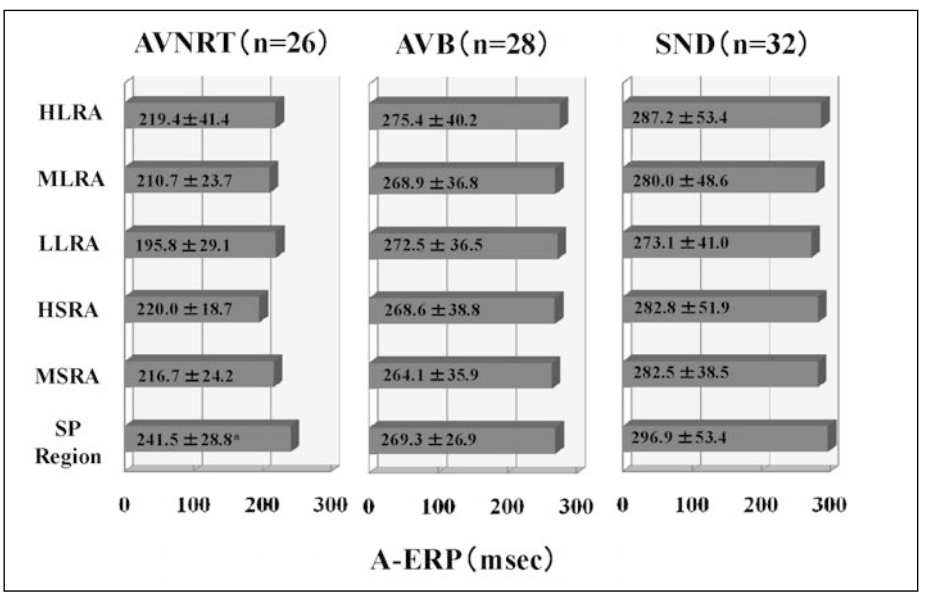

Figure 3. ***The effective refractory periods at the six sites in the right atrium (RA) in patients with atrioventricular nodal reentrant tachycardia, atrioventricular block and sinus node dysfunction.***
The atrial effective refractory periods (A-ERP) with atrioventricular nodal reentrant tachycardia (AVNRT), intra- and infra-Hisian atrioventricular block (AVB) without episodes of any atrial tachyarrhythmias, and sinus node dysfunction (SND) were shown.
HLRA: high lateral RA, MLRA: mid lateral RA, LLRA: low lateral RA, HSRA: high septal RA, MSRA: mid septal RA, SP: slow pathway.

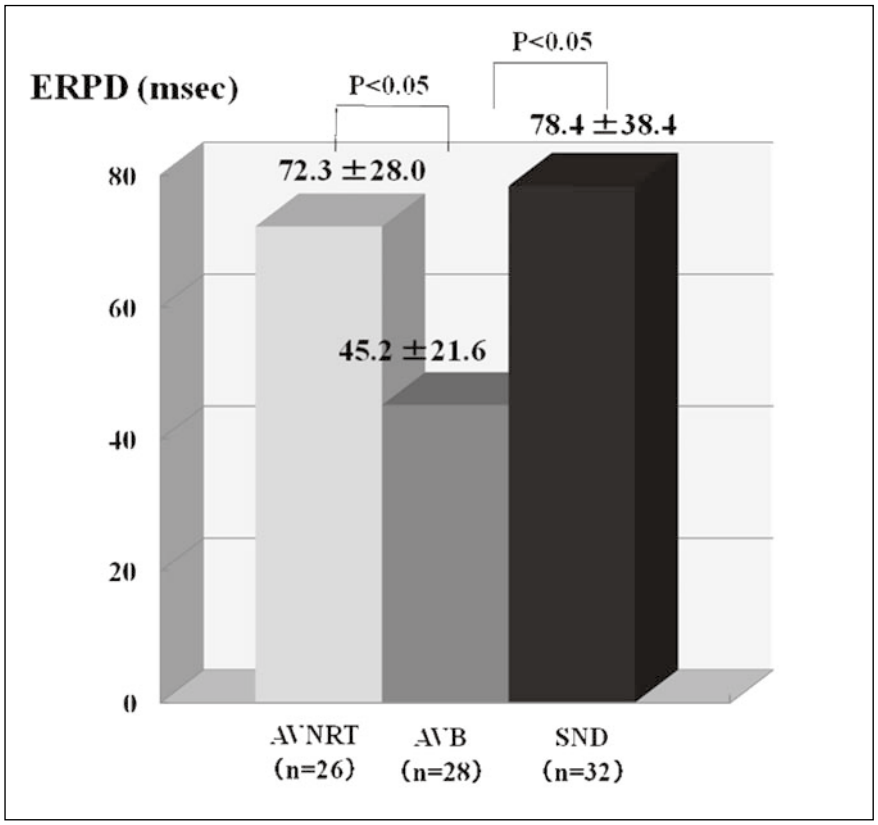

Figure 4. ***Comparison of dispersion in the effective refractory periods in the right atrium among the patients group.*** *Dispersion in the effective refractory periods (ERPD) in patients with atrioventricular nodal reentrant tachycardia (AVNRT) was similar to that in patients with sinus node dysfunction (SND), and there was a significant difference in the ERPD between patients with AVNRT and SND comparing with patients who had intra- and infra-Hisian atrioventricular block (AVB) without episodes of any atrial tachyarrhythmias (p<0.05).*

Discussion

The major findings of this study was that transient AFL/AF was induced in approximately one third of patients with AVNRT, and the ERPD in the RA was about the same as in patients with SND.

As in previous studies, paroxysmal AFL/AF is frequently observed in patients with AVNRT.[1,6] Before catheter ablation era, Hurwitz et al described that AF was documented in 26% patients with AVNRT during 10 years follow-up.[1] Kimman et al reported that AFL/AF was observed in 17% patients after successful slow and/or fast pathway ablation for AVNRT.[6] In addition, AFL/AF was also frequently induced in patients with AVNRT during EPS in the other previous studies.[2,5,8] Razani et al reported that AF was induced in 8% of patients with AVNRT who did not have a history of AF, and the induction rate was increased to 67% if more aggressive protocol for AF induction was employed.[8] It was not unusual that AVNRT initiates paroxysmal AF in previous studies as well.[4,7] Regarding to the study reported by Sauer et al, AVNRT was induced in 4.3% of patients with paroxysmal AF, and AF was cured by SP ablation for AVNRT without pulmonary vein isolation in most of those patients.[7] This study did not include the patients who had documented clinical episodes of AFL/AF, however, the induction rate of transient AFL/AF during an EPS in this study was similar to those in previous studies.[2,8]

The inducing mechanism of AFL/AF in patients with AVNRT is still not clear. Hurwitz et al suggested that "so-called" remodeling of atrial tissue due to

sustained AVNRT may have caused AF.[1] AF that was degenerated from AVNRT might be related to this mechanism. In this study, we terminated induced AVNRT as soon as possible by atrial or ventricular burst pacing. In some patients of the study subject, AFL/AF was already induced before the first induction of AVNRT (Figure 2), therefore, remodeling of atrial tissue due to sustained AVNRT may be ruled out. Kimman et al emphasized in their report that ablation lesion may have related to the occurrence of AFL/AF as a new arrhythmia after slow and/or fast pathway ablation.[6] However, most of previous studies and our study demonstrated that frequent AFL/AF induction was observed before ablation, therefore, this mechanism is not considerable. Decrease in the vulnerability to pacing-induced AF after SP ablation may have direct or indirect effect on AF substrate.[8] The study suggested the effect of SP ablation on atrial vagal tone.[8] The SP contributes to the reentrant circuit for AVNRT, however, it exists in atrial tissue surrounding the compact atrioventricular node, but not within the compact atrioventricular node itself. Regarding that the SP is an abnormal atrial tissue, it may play a role as slow conduction zone for the other kind of atrial reentrant tachycardia such as AFL/AF. Kimman et al also pointed out that 4 patients had pre-existed type 1 AFL and the AFL was cured with ablation technique for AVNRT,[6] while the other study showed no effect of SP ablation on inducibility of AFL.[2] If so, the ERPD in the RA might be wide in patients with AVNRT.

On the other hand, SND is considered to be an atrial disease which is frequently complicated with AFL/AF. Expanded ERPD in the RA myocardium may be related to the occurrence of AFL/AF as shown in previous studies.[9-13] Our previous report also found that the ERPD was significantly wider in SND if it was compared with that in patients without AFL/AF such as the patients who had only intra-Hisain and infra-Hisian conduction disturbance.[13] This study demonstrated that the ERPD in patients AVNRT was wider comparing to almost the same control group of patients with SND, and the relatively longer A-ERP at the SP region may contribute to the wider ERPD.

Study Limitation

In patients with AFL/AF, the left atrial tissue and pulmonary veins are also arrhythmia origin. We did not discuss about the A-ERP in the left atrium in this study. However, all induced AFL/AF showed that the earliest activation site at the onset was in the RA, not in the coronary sinus. So, induced AFL/AF that was considered to be the left atrium origin was not included in this analysis. Therefore, the results and discussion in this study were reasonable for AFL/AF that was originated from the RA and complicated in the patients with AVNRT. In addition, detail RA mapping to identify the reentrant circuit of induced AFL/AF employing Halo catheter or electroanatomical mapping system was not performed in this study, therefore, it was not proved that prolonged A-ERP at the SP region and relatively wide ERPD in the RA was directly related to the occurrence of AFL/AF.

The results of this study were potentially influenced by several factors. This study was not controlled study. The patients with AVB were not "true" control group. Regarding to the A-ERP in the patients with AVB, those were relatively longer comparing with the patients with AVNRT. It indicated that the patients with AVB could not be treated as "a normal RA group". Long lasting bradycardia, artificial pacing and heart failure may have caused atrial electorophisiologic change and affected on the results of this study. The data should have been compared with that in the "true" control group with completely normal heart such as younger patients who underwent an EPS for evaluation of syncope unknown origin, however, obtaining ERPD data from comparable number of such patients was very difficult in the clinical setting. Therefore, we carefully selected these patients as a patients group that had not AFL/AF minimizing the potential impacts on the study results other than unavoidable age difference due to general patient population as shown in Table 1, and the comparison in this study was considered to be also meaningful. Pacing maneuver and induction of AVNRT may have also influenced on the A-ERP.

Therefore, the measurement of A-ERP was already completed before routine EPS was done without any pharmacological interventions. If AVNRT was induced during the measurement of A-ERP, it was immediately terminated as described in the methodology.

The number of patients in the study was relatively small, so further patients collection was required for more discussion such as relationship to induced and especially clinical AFL/AF.

Conclusion

The A-ERP in the RA surrounding the SP was relatively prolonged and the ERPD in patients with AVNRT was as wide as in patients with SND. These atrial electophysiologic abnormalities might be potentially arrythmogenic for atrial tachyarrythmias in patients with AVNRT despite unuseful AV nodal modification.

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