Inducibility of Atrial Flutter in Patients With Atrioventricular Nodal Reentrant Tachycardia

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Background Previous studies have shown that both atrioventricular nodal reentrant tachycardia (AVNRT) and atrial flutter (AFL) have an area of slow conduction located in the low posterior right atrium near the ostium of the coronary sinus. The aim of this study was to evaluate the inducibility of AFL in patients with AVNRT.

Methods and Results One hundred and seventy patients were prospectively evaluated for inducibility of tricuspid valve–inferior vena cava isthmus-dependent AFL. Two groups of patients were analyzed: 71 patients with inducible AVNRT and 99 control patients without a history of AFL. AFL was induced in a greater percentage of patients with AVNRT (53%) than of control patients (27%, p<0.02). In all 21 patients with AVNRT and inducible AFL before slow pathway ablation, AFL was also inducible after slow pathway ablation. There was no difference in the cycle length of induced AFL before and after ablation.

Conclusions AFL was induced in a greater percentage of patients with AVNRT, suggesting that there may be a common area of posteroseptal perinodal atrium participating in the two-tachycardia circuits. However, radiofrequency ablation of the slow pathway of the AVNRT circuit does not influence the inducibility of AFL.

Key Words: Atrial flutter; Atrioventricular nodal reentrant tachycardia; Coronary sinus morphology; Slow pathway

Previous studies have shown that typical atrial flutter (AFL) is caused by a reentrant circuit confined to the right atrium. Percutaneous catheter mapping studies have shown that the reentrant circuit includes an area of slow conduction bounded on the lateral side by the septal leaflet of the tricuspid valve and the inferior vena cava (lateral isthmus) and on the medial side by the Eustachian valve/ridge and the septal leaflet of the tricuspid valve (medial isthmus) and the coronary sinus ostium and the septal leaflet of the tricuspid valve (septal isthmus). Typical atrioventricular nodal reentrant tachycardia (AVNRT) has a dual atrioventricular (AV) nodal pathway physiology and can be cured by radiofrequency catheter ablation (RFCA). The “slow pathway” is thought to have a predominantly posterior–inferior location between the coronary sinus ostium and the septal leaflet of the tricuspid valve, and the “fast pathway” allegedly starts in the anterior–superior portion of the interatrial septum. On the basis of a postmortem study, Inoue and Becker reported that the human compact AV node contains rightward and leftward posterior extensions, with the rightward extension close to the tricuspid annulus. They concluded that these extensions are involved in “slow pathway” conduction (Fig 1). Furthermore, we recently showed by 3-dimensional reconstruction from intracardiac ultrasonographic images that the coronary sinus is significantly larger in patients with AVNRT than in those without. If the same area is critical for AVNRT and AFL, AFL might be inducible in patients with AVNRT. Therefore, the purpose of this study was to evaluate the inducibility of AFL in patients with AVNRT and to determine if the inducibility of AFL is altered by RFCA of the slow pathway of the AVNRT circuit.

Methods

The subjects of the study were 170 consecutive Japanese patients (80 men, 90 women; mean age 49±16 years) referred to Nihon University Hospital for RFCA of supraventricular tachycardia: 71 patients with inducible AVNRT and 99 control patients consisting of 14 patients with atrial tachycardia, 60 patients with manifest Wolff-Parkinson-White (WPW) syndrome and 25 patients with concealed WPW syndrome. No patient had a history of spontaneous AFL prior to the electrophysiological study. Age, sex and body surface area in the AVNRT group and in the group of patients with other types of supraventricular tachycardia are detailed in Table I. No patient had structural heart disease. Each patient completed a signed consent form for participation in the study and ablation therapy. Twenty four patients with clinical history of AFL (21 men, mean age 67.0±9.2 years) were also included in this study to compare the cycle length (CL) of the AFL.

Electrophysiologic Testing

In all patients, antiarrhythmic drug therapy was discon-
tinued at least 5 half-lives before the procedure. The electrophysiologic study was performed in the fasting state. One deflectable, 20-pole “halo” catheter (Cordis-Webster, Baldwin Park, CA, USA) was introduced via the right femoral vein and positioned around the tricuspid annulus to simultaneously record activation of the lateral wall and low atrial isthmus. Two multipolar, closely spaced (2-mm inter-electrode spacing) electrode catheters (Cordis-Webster) were introduced, one via the right femoral vein and the other via the left femoral vein; these were placed in the right atrial appendage and His bundle area, respectively. A 7F thermistor-equipped quadripolar deflectable ablation catheter with a 4-mm distal electrode (EP Technologies, Mountain View, CA, USA) was placed in the right ventricular outflow tract to be used for programmed electrical stimulation and recording during the ablation procedure. One decapolar electrode catheter (Daig Corp, Minneapolis, MN, USA) was introduced via the right internal jugular vein and placed in the coronary sinus with the proximal electrode pair positioned at the ostium. Intracardiac electrograms and surface ECG from leads I, II, V1 and V5 were displayed simultaneously on a multichannel oscilloscopic recorder (Prucka Engineering) and were recorded at a paper speed of 100–200 mm/s. The filter was set from 30 to 500 Hz. A programmed digital stimulator (Fukuda Denshi) was used to deliver 2.0 ms-long electrical pulses at approximately twice the diastolic threshold. During the electrophysiologic study, incremental atrial and ventricular pacing and atrial and ventricular programmed stimulation with up to 2 extrastimuli were performed to induce tachycardia. If these maneuvers did not result in arrhythmia induction, they were repeated during infusion of isoproterenol at 1–4 μg/min. Incremental atrial pacing from the right atrial appendage, low lateral right atrium and coronary sinus ostium starting from a CL of 300 ms in decreasing increments of 20 ms until achievement of 2:1 atrial capture, was performed to induce AFL in all patients before and after successful catheter ablation.

**RFCA**

Radiofrequency (RF) energy was delivered with a thermistor ablation catheter (7F, EP Technologies) to achieve a tip-tissue interface temperature of 50°C at a power setting of 40 W for slow pathway ablation and 60°C at a power setting of 50 W for other ablations. Slow pathway ablation was performed under electrophysiological guidance targeted to the “slow pathway potential”13,14. The preset duration of each RF pulse was 60 s for slow pathway ablation and 120 s for other ablations. Induction of AVNRT was performed after each RF energy application. The ablation was considered successful when (1) no slow pathway conduction was present or single echo beat with jump-up was induced with double atrial extrastimuli during infusion of isoproterenol for AVNRT or (2) atrial tachycardia was no longer inducible or (3) when no antegrade and retrograde accessory pathway conduction was present in patients with WPW syndrome even during infusion of isoproterenol.

**Definition of AFL**

Typical AFL was defined as AFL exhibiting either counterclockwise or clockwise activation around the tricuspid annulus in the right atrium (Fig 2) lasting more than 3 min and concealed entrainment was observed with pacing from the septal or lateral isthmus. AFL lasting more than 5 min was terminated by rapid atrial pacing from the coronary sinus ostium.

**Statistical Analysis**

All data are expressed as mean±SD. The Mann-Whitney U test was used to analyze differences in the clinical, echocardiographic and electrophysiological variables between the AVNRT group and in the control group. The chi-square test for independence and multivariate logistic regression analysis were used to test for association between induc-

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**Table 1 Clinical Characteristics of 170 Study Patients With and Without AVNRT**

<table>
<thead>
<tr>
<th>AVNRT (n=71)</th>
<th>Control (n=99)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.3±15.5</td>
<td>46.1±16.5</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>28/43</td>
<td>52/46</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.46±0.48</td>
<td>1.52±0.55</td>
</tr>
</tbody>
</table>

AVNRT, atrioventricular node reentrant tachycardia; BSA, body surface area.
bility of AFL, and clinical, echocardiographic and electrophysiological variables. Statview 5.0 software was used for statistical analysis (Abacus Concepts, Calabasus, CA, USA) and \( p<0.05 \) was considered significant.

### Results

#### Clinical Characteristics

Patients with AVNRT were significantly older than control patients (52.3±15.5 vs 46.1±16.5 years, \( p=0.0162 \)). In addition, the percentage of females was larger in this group (60.6% vs 46.5%, \( p=0.0135 \)), and body surface area was smaller (1.46±0.48 vs 1.52±0.55 m², \( p=0.0187 \)) (Table 1).

Patients with a clinical history of AFL were significantly older than the AVNRT patients with inducible AFL (\( p<0.0001 \)). Those with clinical history of AFL were significantly more likely to be male (87.5% vs 39.4%, \( p<0.0001 \)).

#### Echocardiographic and Electrophysiologic Characteristics

Transthoracic echocardiography showed the left atrial dimension to be significantly larger in control patients than in the AVNRT patients (31.7 mm vs 28.5 mm, \( p<0.02 \), Table 2). P wave duration on the 12-lead ECG, the atrio-His (AH) and His-ventricular intervals, effective refractory period of the right atrium and interatrial conduction time (pacing stimulus to distal coronary sinus) did not differ between the AVNRT patients and the control patients (Table 2).

### Table 2 Echocardiographic and Electrophysiological Characteristics of Patients With and Without AVNRT

<table>
<thead>
<tr>
<th></th>
<th>AVNRT</th>
<th>Control</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD (mm)</td>
<td>28.5±4.4</td>
<td>31.7±5.7</td>
<td>0.0179</td>
</tr>
<tr>
<td>AH interval (ms)</td>
<td>100.9±32.1</td>
<td>98.8±25.6</td>
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<tr>
<td>HV interval (ms)</td>
<td>46.0±9.5</td>
<td>43.5±9.3</td>
<td>0.1058</td>
</tr>
<tr>
<td>P-wave duration (ms)</td>
<td>119±22</td>
<td>120±20</td>
<td>0.1193</td>
</tr>
<tr>
<td>IACT (ms)</td>
<td>101±20.8</td>
<td>101.7±20.1</td>
<td>0.5725</td>
</tr>
<tr>
<td>EPR RA (ms)</td>
<td>194±29.9</td>
<td>186.5±30.7</td>
<td>0.0857</td>
</tr>
<tr>
<td>AFL inducibility</td>
<td>38/71 (53%)</td>
<td>27/99 (27%)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

LAD, left atrial diameter; AH, atrio-His; HV, His-ventricular; IACT, interatrial conduction time; EPR, effective refractory; RA, right atrium; AFL, atrial flutter. Other abbreviation see in Table 1.

### Table 3 Univariate and Multivariate Analysis of Echocardiographic and Electrophysiological Parameters, and Type of Tachycardia Associated With Induction of AF

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>( p ) value</td>
<td>OR</td>
</tr>
<tr>
<td>Age</td>
<td>0.0281</td>
<td>3.072</td>
</tr>
<tr>
<td>Gender</td>
<td>0.7066</td>
<td>1.092</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>0.2301</td>
<td>1.040</td>
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<tr>
<td>AH interval (ms)</td>
<td>0.1594</td>
<td>1.099</td>
</tr>
<tr>
<td>HV interval (ms)</td>
<td>0.3685</td>
<td>0.985</td>
</tr>
<tr>
<td>EPR RA (ms)</td>
<td>0.4376</td>
<td>0.999</td>
</tr>
<tr>
<td>Type of tachycardia</td>
<td>0.0006</td>
<td>3.071</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval. Other abbreviations see in Table 2.
Mean number of RF ablation for the slow pathway was 5±2 (2–10). AFL was induced in a significantly greater percentage of patients with AVNRT (53%) than in control patients (27%) (p=0.005, Table 2). Univariate analysis was performed to identify clinical, echocardiographic and electrophysiological variables related to inducibility of AFL (Table 3). Inducibility of AFL was shown to be related to age ≥49 years (p=0.028) and to AVNRT (p=0.0006). Multivariate logistic regression analysis was performed to test the statistical significance of age and type of tachycardia in predicting the inducibility of AFL. Of these 2 variables, only the type of tachycardia was shown to be an independent predictor of induction of AFL (Table 3). CLs of the AFL in patients with AVNRT (202.8±19.5 ms, n=21) were significantly shorter than those in patients with clinical history of AFL (counterclockwise AFL: 235.4±24.1 ms, n=17; clockwise AFL: 236.8±21.9 ms, n=9, p<0.0001)

Effects of RFCA
A subgroup of 21 patients with AVNRT in whom RFCA of the slow pathway was successful underwent repeat atrial overdrive pacing at the end of the procedure. In 11 of these 21 patients, no dual AV nodal physiology was present and in 10 of the 21 patients, a single echo beat was present. There was no difference in the inducibility of AFL before (21/21 patients) and after (21/21 patients) slow pathway ablation. The mean AFL CL before ablation (202.8±19.5 ms) did not differ from that after ablation (208.0±36.4 ms) (Table 4).

Discussion
Major Finding
The main finding of this study was a significant association between the inducibility of AFL and AVNRT. AFL was induced in 53% of patients with AVNRT without prior clinical documentation of AFL. This inducibility rate was much higher than that in other patients referred for electrophysiological evaluation and catheter ablation, which indicates that the tachycardia circuits of AVNRT and AFL may have a common substrate. The CL of AFL was significantly shorter in patients with AVNRT than those with clinical history of AFL. The reason for the longer CL in patients with clinical history of AFL might be related to aging and slower conduction time across the cavotricuspid isthmus.

Results of Previous Studies
A previously reported study showed that AFL was more inducible in patients with AVNRT (88%) and in those with a history of AFL (92%) than in control patients (36%) (p=0.0001). The inducibility rate we observed (53%) was much lower than that reported by Kalbfleisch et al but was similar to that reported by a prior study in which AFL was induced in 13 of 24 patients (54%) with AVNRT. The difference between our study results and those of Kalbfleisch et al may be related to the more aggressive pacing protocols used by Kalbfleisch et al who paced down to a CL of 100 ms. Thus, the results of our study, together with the results of previous studies indicate that in patients with inducible AVNRT and inducible AFL, the tachycardia circuits may share a common area of perinodal atrium.

Effect of RFCA on Inducibility of AFL
A preliminary report suggested that AFL is commonly inducible in patients with a history of AVNRT and that RF energy applied to the tricuspid annulus above the coronary sinus ostium often eliminates the inducibility of both circuits. However, the present study and a previous study did not find this to be the case. Successful ablation of AVNRT by delivering RF energy posterior to the His bundle position near the coronary sinus ostium had no effect on the percentage of patients with inducible AFL. This observation suggests that the critical area in the perinodal atrium for AFL and AVNRT may differ; that is, the 2 tachycardia circuits do not actually use a common portion of the perinodal atrium. Another possibility is that abolishing AVNRT requires less destruction to this area than is required to inhibit the inducibility of AFL. The latter possibility is supported by well-known data showing that patients may still have evidence of slow pathway function but no inducible AVNRT after successful modification of the AV node by ablation of the slow pathway. Conversely, Tai et al and Zimmerman et al reported that RF catheter ablation of the cavotricuspid isthmus was effective in eliminating typical AFL without disturbance of antegrade fast AV node conduction, but prolongation of the AV node Wenkebach CL and maximal AH interval and elimination of dual AV nodal function in patients with dual AV nodal pathway physiology. These studies provide evidence that the atrial musculature in the cavotricuspid isthmus significantly contributes to the slow AV node conduction.

Study Limitations
First, the predictive value of inducible AFL has not been evaluated in this study. A recent study reported that 1 patient without a previous history of AFL (1/47) suffered from typical AFL during long-term follow-up (9.3±3 years) after successful RFCA of the slow pathway for AVNRT. But induction of AFL was not performed in those study patients. Second, the present patients with AVNRT were significantly older than the control patients. However, a previous report on RF ablation for AFL had a mean age of 63±10 years and male predominance (76 males, 28 females) so our AVNRT patients (52.3±15.5 years old, females: 60.6 %) differed from the typical AFL population.

Conclusion
There is an association between the inducibility of AVNRT and AFL, which together with evidence from previous studies implies that there may be a pathologic or mechanistic link between these 2 arrhythmias. However, our results showed that inducibility of AFL following slow pathway ablation for AVNRT was unaltered. Thus, even if both arrhythmias have a common area of the perinodal atrium in their tachycardia circuit, the width of the AFL circuit at the septal cavotricuspid isthmus should be larger than slow pathway location because of the wider, “windsock” appearance of the coronary sinus ostium in patients with AVNRT. However, inducibility of AFL in patients with AVNRT may not predict spontaneous onset of AFL in the future.

References

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AVNRT and AFL


