Title: Distribution of the Origin of Adenosine Triphosphate-Sensitive Atrial Tachycardias With the Earliest Activation Recorded in the His Bundle Catheter

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Background: The aim of this study was to assess the spatial distribution of the origins of adenosine triphosphate (ATP) sensitive focal atrial tachycardias (AT) that have their earliest activation recorded in the His bundle (HB) catheter.

Methods and Results: Catheters were placed according to the standard fashion for an electrophysiologic study of supraventricular arrhythmia, namely, high right atrium, HB, coronary sinus, and right ventricle. The ATs with their earliest activation recorded in the HB catheter and that were terminated by rapid injection of ATP (4.3 ± 2.5 mg), formed the study group (n = 12). After catheter ablation of these ATs, the distances between the successful ablation site and the HB area were measured. Only one successful site was near the HB and the other sites were at the noncoronary sinus of Valsalva (n = 6), tricuspid annulus (n = 3), right atrial septum (n = 1), and left atrial septum (n = 1). The average distance between the HB catheter and successful site was 10.4 ± 8.8 mm. In 5 of the 12 cases (the 3 tricuspid and 2 septal foci), the distances were greater than 10 mm.

Conclusions: When ablating ATP-sensitive AT with the earliest activation recorded in the HB catheter, it is important to perform detailed mapping not only around the HB. (Circ J 2013; 77: 626–631)

Key Words: Adenosine triphosphate; Atrial tachycardia; Catheter ablation; His bundle area

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ne of the conventional strategies for ablating focal atrial tachycardia (AT) with radiofrequency (RF) energy is to seek and target the site of earliest activation. This involves conducting detailed baseline mapping within the atrium, and analyzing the sequence of atrial activation of the AT recorded by the intracardiac electrode catheters. For AT originating from the His bundle (HB) area, mapping is carefully performed in the area around the HB. However, the origin of the AT can be distant to the HB area, even if the site of earliest atrial activation among the high right atrium (HRA), HB, and coronary sinus (CS) catheters is observed in the HB catheter. In those cases, meticulous mapping around the HB area may prolong the procedure without helping the operator to achieve ablation success. Adenosine-sensitive AT in which the earliest activation is recorded at the HB is considered to be among ATs arising from the atrioventricular (AV) annulus, but the distribution and actual distance between the HB and successful ablation sites has never been evaluated.

Therefore, the objective of this study was to assess the distance between the HB area and successful site of ablation of ATs in which the earliest activation sites were recorded by the HB catheter, among the standard HRA, HB and CS catheters, and their spatial distribution.

Methods

Patients’ Characteristics

The records of 41 patients who underwent electrophysiologic study (EPS) and ablation of focal ATs from 2004 to 2011 were reviewed and 12 patients (29%) in whom the AT was terminated by rapid injection of a small amount of adenosine triphosphate (ATP) and in whom the earliest atrial activation during AT was recorded in the HB catheter among the standard HRA, HB and CS catheters were investigated in this study.
Structural heart disease was defined using a history of prior open-heart surgery and echocardiographic criteria, namely, presence of left ventricular (LV) asynergy, reduced LV ejection fraction, abnormal LV hypertrophy, aortic and mitral valve disease, or left atrial dilatation.

Verbal and written informed consent for the ablation procedure and study was given by all patients prior to the procedure. The study protocol, including data collection and record keeping, was approved by the hospital’s institutional review board.

Table 1. Patients’ and Tachycardia-Related Characteristics

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, years</th>
<th>Sex</th>
<th>Structural heart disease</th>
<th>TCL, ms</th>
<th>ATP, mg</th>
<th>Successfull ablation site</th>
<th>AbA-HisA, ms</th>
<th>Ab-HBE, mm</th>
<th>AbA-P, ms</th>
<th>Inverse relationship in tachycardia induction</th>
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<td>366</td>
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<td>F</td>
<td>Post AVR</td>
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<td>5</td>
<td>SEP sup</td>
<td>35</td>
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<td>24</td>
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<td>58</td>
<td>M</td>
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<td>270</td>
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<td>SEP mid</td>
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</table>

Mean 63.1±12.6 355.2±55.2 4.3±2.5 24.7±16.5 10.4±8.8 24.7±15.8

AbA-HisA, time difference between atrial electrograms of the successful ablation point and His bundle catheter; AbA-P, time difference between atrial electrograms of the successful ablation point and onset of P-wave in lead II of surface ECG; Ab-HBE, distance between successful ablation site and His bundle area; ant, anterior; ATP, adenosine triphosphate; AVR, aortic valve replacement; HBA, His bundle area; mid, middle; NCS, noncoronary sinus of Valsalva; PLSVC, persistent left superior vena cava; SEP, atrial septum; sep, septal; sup, superior; TA, tricuspid annulus; TCL, atrial tachycardia cycle length.

Origin of ATP-Sensitive ATs

ATP (Adetphos-L, Kowa, Nagoya, Japan) was given as an intravenous bolus injection during the AT in increasing amounts from 2 mg to 10 mg until termination of the AT.

During the AT, the time between the atrial potential recorded by the HB catheter and the onset of the surface P-wave in lead II was measured.

Definitions

Standard electrophysiological techniques were used to exclude diagnoses of an accessory pathway or AV nodal reentrant tachycardia. A diagnosis of focal AT was made using the following conventional criteria: (a) abnormal P-wave morphology during the tachycardia, (b) endocardial atrial activation sequence during AT inconsistent with sinus origin and unable to be reproduced by ventricular stimulation, (c) tachycardia induction by ventricular stimulation associated with V-A-A-V sequence, (d) no evidence of a macroreentrant atrial tachycardia, (e) change in the A-A interval during tachycardia preceding any change in the V-V interval, (f) presence of AV conduction block or delay without affecting tachycardia cycle length, (g) dissociation of ventricular activity from the tachycardia, (h) tachycardia initiation independent of a critical prolongation of the AH interval, and (i) termination of the tachycardia without blocking AV nodal conduction. In the patients in whom an electroanatomical mapping system was used, focal AT was defined as follows: (a) conduction pattern radiating in all directions from a single site of earliest activation, and (b) range of activation times less than the tachycardia cycle length.

Catheter Ablation

RF energy was applied at the site of earliest bipolar activation (maximal temperature: 55°C, duration: 60 s, power: 40 W). The location of the RF energy application was recorded by fluoroscopy and stored for further evaluation, together with the intracardiac electrogams, on an electrophysiological recording system (LabSystem PRO EP recording system, C.R. Bard, Inc, Lowell, MA, USA). When an electroanatomical mapping system was used, ablation tags were marked on the 3D recon-
The mean tachycardia cycle length was 355.2 ± 55.2 ms. The remaining 3 were on 2 of the 3 types of drugs. ± 24.7 was same or earlier than the onset of the surface P-wave for the atrial potential recorded by the HB catheter during the AT. The atrial potential recorded by the HB catheter in all patients as per our study inclusion criteria. The earliest atrial activation during the AT was recorded by the class I antiarrhythmic drug, and (patient nos. 4 and 6), and 1 on all 3 types of drugs (verapamil, only (patient no. 9), 2 on class I antiarrhythmic drugs only (patient no. 5), 3 on class II antiarrhythmic drugs (patient nos. 6 and 11). The activation map acquired by the CARTO system shows a centrifugal conduction pattern. The activation map acquired by the CARTO system shows a centrifugal conduction pattern.

The “HB area” was defined as the interelectrode area where the HB potential was recorded within the HB catheter. In patients for whom an electroanatomical mapping system was used, the distance between the successful ablation site and the HB area was measured by the system. In other patients, the measurement was made under fluoroscopic guidance.

### Measurement of the Distance

The distance between the successful ablation site and the HB area averaged 10.4 ± 8.8 mm (range 4–35 mm). The average time by which the atrial potential recorded at the successful ablation site preceded that of the HB catheter was 24.7 ± 16.4 ms (range 0–61 ms). Table 2 summarizes these distance and time differences by site and Figure 1 illustrates the spatial distribution of the foci.

![Figure 1](image.png)

**Figure 1.** Illustration of successful ablation sites in 12 patients with ATP-sensitive atrial tachycardia. Successful ablation was at the noncoronary sinus of Valsalva (NCS) in 6 patients, anterior tricuspid annulus (TA) in 2 patients, septal TA in 1 patient, immediate vicinity of the His bundle (HB) area in 1 patient, right atrial (RA) septal wall in 1 patient and left atrial (LA) septum in 1 patient. Red symbols indicate the successful ablation sites <10 mm from the HB area, black >10 mm. ATP, adenosine triphosphate; LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle.

### Statistical Analysis

Continuous data are expressed as mean ± SD.

### Results

#### Patients’ Characteristics

Clinical and tachycardia characteristics of the 12 patients are listed in Table 1. The mean age was 63.1 ± 12.6 years and 8 of the 12 patients were female (66.7%). One patient had a history of open-heart surgery and another patient had persistent left superior vena cava. None of others had structural heart disease. The drugs being taken by the patients prior to the ablation session were recorded: 5 patients were not taking cardiovascular drugs (patient nos. 1, 3, 5, 10, and 12), 1 on verapamil only (patient no. 9), 2 on class I antiarrhythmic drugs only (patient nos. 4 and 6), and 1 on all 3 types of drugs (verapamil, class I antiarrhythmic drug, and β-blocker: patient no. 11). The remaining 3 were on 2 of the 3 types of drugs.

#### Electrophysiological Characteristics

The mean tachycardia cycle length was 355.2 ± 55.2 ms. The earliest atrial activation during the AT was recorded by the HB catheter in all patients as per our study inclusion criteria. The atrial potential recorded by the HB catheter during the AT was same or earlier than the onset of the surface P-wave for 24.7 ± 15.8 ms (range 0–45 ms).

Likewise, injection of ATP terminated the sustained AT in all patients. The mean dosage of ATP required for AT termination was 4.3 ± 2.5 mg (range 2–10 mg). In 2 of 12 patients, relatively larger amounts of ATP (8 and 10 mg, respectively) were used compared with previous reports. Nevertheless, because all tachycardias were terminated without blocking AV conduction, they were defined as ATP-sensitive AT.

An inverse relationship between the coupling interval of the extrastimulus initiating the AT and the interval from the stimulus to the first complex of the AT was observed in 8 patients, which suggested microre-entry to be the mechanism (patient nos. 1, 2, 3, 5–8, and 10). In the remaining 4 patients, the relationship was not assessed.

### Successful Ablation Site

Catheter ablation was successful in all 12 patients. There was only one patient in whom the successful ablation site was in the immediate vicinity of the HB. In 6 patients, the earliest activation was obtained at the noncoronary sinus of Valsalva (NCS) and ablations performed there were successful in terminating the AT. In the remaining 5 patients, the successful ablation site was at the tricuspid annulus (TA, n=3) or at the atrial septum far from the AV junction (n=2).

The distance between the successful ablation site and the HB area averaged 10.4 ± 8.8 mm (range 4–35 mm). The average time by which the atrial potential recorded at the successful ablation site preceded that of the HB catheter was 24.7 ± 16.4 ms (range 0–61 ms). Table 2 summarizes these distance and time differences by site and Figure 1 illustrates the spatial distribution of the foci.

Table 1. Distance From the HB to the Successful Ablation Site and the Interval Between the Atrial Electrograms Recorded at the Successful Ablation Site and the HB*

<table>
<thead>
<tr>
<th>Successful ablation site</th>
<th>n</th>
<th>Distance (mm)</th>
<th>Time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricuspid annulus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>2</td>
<td>14.5±2.1</td>
<td>18.0±14.1</td>
</tr>
<tr>
<td>Septal</td>
<td>1</td>
<td>14</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>14.3±1.5</td>
<td>25.0±15.7</td>
</tr>
<tr>
<td>Noncoronary sinus</td>
<td>6</td>
<td>5.2±1.5</td>
<td>23.5±21.1</td>
</tr>
<tr>
<td>HB area</td>
<td>1</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Atrial septum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>1</td>
<td>11</td>
<td>35</td>
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<tr>
<td>Left</td>
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<td>35</td>
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</table>

*Note that all sites other than the noncoronary sinus and the HB area were separated from the HB by >10 mm.

HB, His bundle.
Origin of ATP-Sensitive ATs

Distribution of the AT
Several years ago, Iesaka et al. reported on the existence of adenosine-sensitive atrial microreentrant tachycardia that arose near the HB. They speculated that the AV node or its transitional tissues were part of the reentrant circuit. Since then, it has been found that the foci of such adenosine-sensitive microreentrant ATs may also arise at diverse sites such as the CS ostium, TA, mitral annulus, and others.

In our study, 6 of 12 ATs were terminated by RF application at the NCS. The distances between the ATs and the HB area were short (5.2±1.5 mm). Ablating at the NCS is a well-known strategy for this type of AT and has been reported by several authors. The RF energy from the site may penetrate through the atrial septum and may be able to ablate the tachycardia circuit without damaging the HB. However, another 3 foci existed along the TA, which may have been caused by AV nodal tissue extending along the AV junction. As shown in Table 2, the foci at the TA were separated from the HB area by an average of 14.3±1.5 mm. It is important to note that the earliest atrial activation was nevertheless recorded by the HB catheter, because the catheters are not placed around the TA in a standard EPS. Therefore, ATs arising from the TA may sometimes be misidentified as para-Hisian AT. The mechanisms of the 2 ATs originating from the atrial septum (1 left-, 1 right-sided) were unclear because detailed EPS were not performed. This type of septal AT may also be misdiagnosed as a para-Hisian AT, because again, the standard catheters are not placed around the TA. As described in patient no. 7 (Figure 2), 3D electroanatomical mapping was helpful for detailed mapping during AT.

Mechanism of ATP-Sensitive AT
In our present study, 10 of 12 ATs (83.3%) arose from the AV junction. The special nature of the tissue around the junction may play an important role in the occurrence of these ATs. Several investigator have studied the characteristics of AV junctional tissue and have found that it resembles atrial myocardiun histologically and extends along the AV valvular annulus. However, electrophysiologically, it resembles AV nodal tissue, including its response to adenosine. ATP is rapidly broken down into adenosine in the bloodstream, with a plasma half-life of less than 1s. As a consequence, an intravenous dose of ATP may reach the site of action as adenosine. The effects of adenosine on supraventricular tissue include shortening of the action potential duration mediated by a potassium current (IK_Ach), and antiadrenergic electrophysiological effects resulting from inhibition of adenyl cyclase, which leads to a reduction of the inward L-type calcium current (ICa_L). Therefore, adenosine may transiently terminate conduction through the AV node or inhibit delayed afterpotentials in atrial tissue, which could lead to catecholamine-induced triggered activity.

Iesaka et al were the first to report that the circuit of ATP-sensitive microreentrant AT might include AV nodal tissue, according to their speculation that the conduction block in the circuit was induced by reduction of the inward calcium current, an effect of ATP. On the other hand, Iwai et al examined the response of 43 patients with AT to adenosine and reported that all focal AT were terminated by rapid injection of adenosine, except for those whose etiologies were due to macroreentry. More recently, based on electrophysiological behavior and response to drugs, they suggested that para-Hisian AT was mechanistically consistent with triggered activity. Further investigation is needed to elucidate the mechanism of this type of AT.

In our study, 8 patients had an inverse relationship between the coupling interval of the extrastimulus initiating the AT and the interval from the stimulus to the first complex of the AT.
In ATP-sensitive AT that have the earliest activation recorded in the HB catheter among the HRA, HB and CS catheters placed according to the standard fashion for an EPS of supraventricular arrhythmia, it is important to perform detailed mapping not only around the HB, but also the TA and both sides of the septum.

**Disclosures**

There is no source of financial support and no conflicts of interest.

**References**

1. Iesaka Y, Takahashi A, Goya M, Soejima Y, Okamoto Y, Fujiwara H,


