Usefulness of Non-contact Mapping for Radiofrequency Catheter Ablation of Inappropriate Sinus Tachycardia: New Procedural Strategy and Long-term Clinical Outcome

Masao Takemoto¹, Yasushi Mukai¹, Shujiro Inoue¹, Tetsuya Matoba¹, Mari Nishizaka¹, Tomomi Ide¹, Akiko Chishaki² and Kenji Sunagawa¹

Abstract

**Objectives** The present study evaluated the clinical benefits of a new therapeutic method of radiofrequency catheter ablation (RFCA) using an EnSite system for inappropriate sinus tachycardia (IST).

**Materials and Methods** Six patients with debilitating IST underwent RFCA using EnSite. Using the beta-adrenergic blocker and agonist, the heart rate was controlled between 70 to 150 bpm before and after the RFCA. The areas of the breakout sites (BOSs) were clearly distinguished between those from the normal P-wave zones during rates of less than 100 bpm and those from more upper rate sites during rates of more than 100 bpm using the EnSite system, in accordance with the appearance of tall P-waves (tall P-wave zone) in the IST patients. This was selected as the target for ablation.

**Results** After the RFCA, the BOSs observed during heart rates of more than 100 bpm moved completely from the tall P-wave zone to the normal P-wave zone in the IST patients. The total number of heart beats and average heart beat on the 24-h Holter monitoring decreased statistically from that before the RFCA to that after, and no adverse heart rate responses was observed after the RFCA. Before the RFCA, the brain natriuretic peptide was elevated, New York Heart Association functional class was worse, and there was an impaired exercise tolerance observed with exercise electrocardiogram testing. The RFCA for the IST significantly improved those parameters.

**Conclusion** This new therapeutic method for IST using EnSite is effective and produces clinical benefits.

Key words: inappropriate sinus tachycardia, non-contact mapping, catheter ablation

(DOI: 10.2169/internalmedicine.51.5882)

Introduction

Inappropriate sinus tachycardia (IST) is an uncommon clinical syndrome that is characterized by an elevated resting heart rate or disproportionate increase in the rate with minimal exertion (1). This condition is predominantly encountered in women and common symptoms include palpitations, presyncope/syncope, chest pain, dizziness, shortness of breath, anxiety and depression (2). Radiofrequency (RF) catheter ablation (RFCA) is an acceptable treatment modality for drug refractory IST, and several procedural strategies for sinus node (SN) modification have been described (1-3). Here we report our new observations using a non-contact mapping system, EnSite (St. Jude Medical, Minnetonka, MN, USA) in patients with drug refractory IST.

Materials and Methods

**Study population and laboratory analysis**

From 2006 to 2009, 6 consecutive patients (3 males and 3 females with a mean age of 43 ± 3 years old) with drug refractory (including beta-blockers, calcium-channel blockers,
and digitalis) IST underwent RFCA in our hospital. All patients had their history recorded, and underwent a physical examination, laboratory analysis, chest X-ray, 12-lead electrocardiogram, 24-h Holter monitoring, M-mode, two-dimensional and Doppler echocardiograms, and exercise electrocardiogram testing on admission or within at least 1 month before the admission, and 2 or 3 days after the RFCA. These examinations yielded no evidence of clinically overt structural heart disease, including coronary artery disease, valvular heart disease, congenital heart disease, LV hypertrophy, or RV abnormalities in any of the patients. The serum brain natriuretic peptide (BNP) concentration and New York Heart Association (NYHA) functional class were evaluated on admission and 6 to 12 months after the RFCA. The mean follow-up period was 29 ± 2 months.

**Definition of IST**

IST was defined as: 1) a P-wave axis and morphology during the tachycardia similar to that during sinus rhythm, and tall P-waves during the tachycardia which were at least 2-fold taller than those during sinus rhythm, especially in leads II, III, and aVF, 2) a heart rate of greater than 100 beats per minute (bpm) at rest or with minimal exertion, 3) exclusion of any secondary causes of tachycardia, 4) 24-h Holter monitoring demonstrating a mean heart rate of greater than 90 bpm, and 5) a heart rate of greater than 130 bpm within the first 90 seconds of a standard Bruce protocol on the treadmill test (1, 4, 5).

**Mapping and catheter ablation procedure**

All procedures were performed after written informed consent was obtained. The patients were studied in the fasting state without sedation. Antiarrhythmic drugs and beta-blockers were discontinued for at least five half-lives before the procedure, intravenous heparin was given as a 5,000-unit bolus dose. Using an intravenous administration of the beta-adrenergic blocker, landiolol (5 to 40 μg/kg/min) and agonist, isoproterenol (ISP) (2 to 5 μg intravenous administration), the heart rate was controlled between 70 to 150 bpm before and after the RFCA. Then, the origins which indicated the SN during sinus rhythm and IST were defined as the earliest sites showing a single spot on the isopotential map and a QS pattern in the noncontact unipolar electrograms, as previously described (6). The breakout sites (BOSs) during sinus rhythm and IST were also defined as the earliest sites that showed an rS pattern with a sudden increase in the peak negative potential of the noncontact unipolar electrogram. These origins and BOSs were tagged for each heart rate on the RA geometry (Fig. 1C-H, 2A-J). In all patients, compared to that during heart rates of less than 100 bpm with normal P-waves (normal P-wave zone), the BOSs steadily moved to more upper rate sites during heart rates of more than 100 bpm in accordance with the appearance of tall P-waves (tall P-wave zone) (Fig. 1C-J, 2A-J). The SN and BOSs within normal P-wave zones and tall P-wave zones could easily and clearly be separated by this method. The RF energy was delivered to the tall P-wave zones, and not to the SN or normal P-wave zones, for 30 to 60 seconds with a preset temperature of 50°C and power limit of 30W. In 4 of 6 patients, repetitive atrial response was observed. The average distance between SN and ablation site was 12.7 ± 0.7 mm. A successful RFCA was defined as that when the BOSs observed during heart rates of more than 100 bpm (100 to 150 bpm) moved completely from the tall P-wave zone to the normal P-wave zone (Fig. 2C, D, E, H-J) with and without the intravenous administration of isoproterenol in accordance with the abolishment of the tall P-waves on the 12-lead electrocardiogram during the RF energy delivery (arrows in Fig. 1K). All 12-lead electrocardiograms and the bipolar intracardiac electrograms (filtered at 30 to 400 Hz) were recorded and stored using a 96-channel acquisition system (CardioLabEP, Prucka Engineering Inc., Houston, TX, USA). During the procedure, intravenous heparin was given as a 5,000-unit bolus dose.

**Statistical analysis**

The numerical results are expressed in the text as the mean ± standard deviation. Paired data were compared by a Student’s t test. A value of p<0.05 was considered to indicate statistical significance.

**Results**

**Patient characteristics**

Although patients primarily women in this syndrome, 50% were male in this study. An RFCA procedure for IST was performed in 6 patients. Procedural success was achieved in all 6 (100%) of the patients. No patients suffered from any procedure-related complications including SN dysfunction (sick sinus syndrome), cardiac tamponade, diaphragmatic paralysis, or superior vena cava syndrome. During 1-year follow-up, no recurrence of IST was observed in any of the patients. However, in 1 of the 6 patients the IST recurred and that patient underwent a repeat RFCA with a successful result a year and a half after the first RFCA.
The total number of heart beats and average heart beat statistically differed between that before and that after the RFCA (<0.01) (Table 1). Although the heart rate was greater than 100 bpm at rest or with minimal exertion before the RFCA (Fig. 3A), an adverse heart rate response was not observed after the RFCA (Fig. 3B).

**24-h Holter monitoring** (Table 1)

The total number of heart beats and average heart beat statistically differed between that before and that after the RFCA (<0.01) (Table 1). Although the heart rate was greater than 100 bpm at rest or with minimal exertion before the RFCA (Fig. 3A), an adverse heart rate response was not observed after the RFCA (Fig. 3B).

**Serum BNP concentration and NYHA functional class**

The serum BNP concentration and NYHA functional class were evaluated in all patients on admission and 6 to 12 months after the RFCA. The serum BNP was elevated before the RFCA. However, it significantly decreased 6 to 12 months after the RFCA (<0.05) (Fig. 4A). The NYHA functional class was demonstrated to be significantly worse
Exercise electrocardiogram testing (Table 1)

One of the 6 patients could not perform an exercise electrocardiogram test due to a gait disturbance caused by necrosis of the head of the femur. Compared to that before the RFCA, the resting heart rate significantly decreased after the RFCA (p<0.05). The time to achieve a heart rate of 130 bpm took significantly longer after the RFCA than before (p <0.01). Moreover, the RFCA significantly improved the exercise tolerance of the IST-patients (p<0.05).

Response to beta-adrenergic receptor stimulators (Table 1)

Before the RFCA, a low dose of ISP could steadily increase the patients’ heart rate to 150 bpm. However, compared to that before the RFCA, a high dose of ISP was needed to increase the heart rate to 150 bpm (p<0.01) after the RFCA.

Patient symptoms and medications (Table 2)

On admission, all patients had IST-associated symptoms including palpitations (100%), general fatigue (83%), depression (67%) and fainting (33%). All patients had been taking antiarrhythmic agents before admission, such as beta-blockers (100%), calcium channel antagonists (33%) and digitalis (17%). However, those agents were not sufficiently effective in eliminating the IST-associated tachycardia and symptoms. All of the patients with a successful procedure reported the absence of any IST-associated tachycardia or symptoms after the RFCA. In 4 of the 6 patients it was possible to discontinue those antiarrhythmic agents. Two of the 6 patients continued to receive the beta-blockers for their hypertension.

Discussion

Major findings and clinical implications

The major findings of this study are as follows: 1) in a short time EnSite could steadily and clearly separate the SN, normal P-wave zone, and tall P-wave zone which was the targeted site of the RFCA (Fig. 1C-H, 2A-J), 2) the RFCA could easily and efficaciously treat the IST without any complications, and 3) all patients were free from any further IST-associated tachycardia (Fig. 3A, B) or symptoms (Table 2) in accordance with a decrease in their heart rate (Table 1), and experienced a dramatic improvement in the inappropriate increase in their heart rate with minimal exertion (Table 1), serum BNP level (Fig. 4A), NYHA functional class (Fig. 4B), and exercise tolerance (Table 1). Some previous studies demonstrated that the recurrence rate was 20 to 50% and some patients underwent a pacemaker implantation (1, 3, 7-9). However, with this method, the recurrence rate was only 1 out of 6 patients (17%) during a mean follow-up period of 29 ± 2 months. The characteristic point of this method which differs from that of the previous studies is that the target site of the RFCA was the BOSs in the tall P-wave zone, and not the SN. Thus, the RF energy could safely and easily be delivered at the target sites (BOSs) without any complications. As a result, this method could achieve an acceptable long-term clinical outcome. This method should be a new safe and effective procedural strategy for IST.
Table 1. Parameters before and after Radiofrequency Catheter Ablation

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>24-h Holter Monitoring Analysis (n=6)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total HB (x10^3 beats/day)</td>
<td>134 ± 2</td>
<td>113 ± 2**</td>
</tr>
<tr>
<td>average HB (beats/minute)</td>
<td>93 ± 1</td>
<td>79 ± 1**</td>
</tr>
<tr>
<td><strong>Exercise Electrocardiogram Testing Analysis (n=5)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting HR (beats/minute)</td>
<td>108 ± 2</td>
<td>95 ± 2*</td>
</tr>
<tr>
<td>Time-HR130 (seconds)</td>
<td>76 ± 5</td>
<td>212 ± 5**</td>
</tr>
<tr>
<td>Exercise tolerance (Mets)</td>
<td>6.8 ± 0.4</td>
<td>9.3 ± 0.6*</td>
</tr>
<tr>
<td><strong>Response to Beta-adrenergic Receptor Stimulator (n=6)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISP dose achieved HR150 bpm (μg)</td>
<td>2.8 ± 0.2</td>
<td>4.8 ± 0.3**</td>
</tr>
</tbody>
</table>

**p<0.01, *p<0.05 versus before RFCA, HB = heart beats, HR = heart rate; Time-HR130 = time achieved 130 bpm of the heart rate; ISP = isoproterenol.

Figure 3. The 24-h Holter monitoring before and after the radiofrequency catheter ablation (RFCA). The heart rate was greater than 100 bpm at rest or with minimal exertion before the RFCA (A). However, that adverse heart rate response was not observed after the RFCA (B).

**Mechanism of IST**

Although the mechanism(s) of IST has not been completely elucidated, several potential mechanisms have been raised include the following: 1) autonomic dysfunction including an increased sympathetic tone and/or receptor sensitivity, blunt parasympathetic tone, or sympathovagal imbalance (2, 10), 2) abnormal automaticity of the SN (2, 11), 3) an atrial tachycardia focus near the SN (2), and 4) dysautonomia involving the anterior right ganglionic plexi (ARGP) (12, 13).

In this method, the target of the RFCA sites was the BOSs in the tall P-wave zone, and not the SN, indicating that abnormal automaticity of the SN may not be the potential mechanism of IST (14). The distinction between a focal atrial tachycardia and IST is often difficult to make. Occasionally, this distinction can be made clinically in that atrial tachycardia may not be related to activity with an unpredictable onset of the tachycardia at rest or with minimal exertion. Moreover, the BOSs of the tachycardia shifts for each different heart rate. This point may differentiate IST from focal atrial tachycardia.

It has been reported that epinephrine injected into the ARGP, which is located in the fat pad at the base of the right pulmonary veins adjacent to the caudal end of the SN, induces IST, and ablation of the ARGP eliminated the IST without damaging the SN (12, 13). Since the ablation sites were near the SN in this study, it may be possible that the ARGP may have been ablated. However, we could not sufficiently explain why the BOSs moved from the tall P-wave zone to the normal P-wave zone. Further studies may be needed to explain this.

We assumed that two types of autonomic regulation may exist, because there are two types of BOSs, those associated with a tall P-wave zone and those with a normal P-wave zone. Since the response to beta-adrenergic receptor stimulators differed before and after the RFCA (Table 1), one type of autonomic regulation may be an increased sympathetic tone and/or receptor sensitivity. Thus, the ablation of these abnormal autonomic regulation sites may abolish the IST-associated tachycardia, and improve the response to beta-adrenergic receptor stimulators. As a result, the BOSs shifted from the tall-P wave zone, possibly autonomic regulation sites, to the normal P-wave zone, possibly normal autonomic regulation sites.

**Limitation of this study**

The patient number of this study is comparably small. This arrhythmia involves several mechanisms such as primary sinus node abnormality, depressed efferent cardiac reflex and beta-adrenergic hypersensitivity (11). Not all of the patients with this arrhythmia may show a similar response to landiolol or isoproterenol. The similar trend in the response might occur only in a small subgroup of patients with this arrhythmia.

**Conclusion**

Finally, this new therapeutic method for ablating IST using the EnSite system was effective and safe. Although IST is an uncommon clinical syndrome, it has disabling symptoms. Thus, physicians should be aware of this condition when examining a patient with a tachycardia characterized by an elevated resting heart rate or a disproportionate increase in the heart rate with minimal exertion. Since IST is often drug-refractory, RFCA utilizing EnSite may be considered as the first choice of therapy in such patients.

**The authors state that they have no Conflict of Interest (COI).**

**Acknowledgement**

We thank Ryoko Hayashi, Kou Adachi, Keiji Kobayashi, and Noriko Nakajima for their technical assistance with the electrophysiological studies in the cardiac catheterization laboratory, and John Martin for his linguistic assistance with this paper.
References


Table 2. Patient Symptoms and Medications before and after Radiofrequency Catheter Ablation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>palpitations</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>general fatigue</td>
<td>83%</td>
<td>0%</td>
</tr>
<tr>
<td>depression</td>
<td>67%</td>
<td>0%</td>
</tr>
<tr>
<td>fainting</td>
<td>33%</td>
<td>0%</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>beta-blockers</td>
<td>100%</td>
<td>33%</td>
</tr>
<tr>
<td>calcium-channel blockers</td>
<td>33%</td>
<td>0%</td>
</tr>
<tr>
<td>digitalis</td>
<td>17%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 4. The serum brain natriuretic peptide (BNP) concentration and New York Heart Association (NYHA) functional class before and 6 to 12 months after the radiofrequency catheter ablation (RFCA). The serum BNP level was elevated before the RFCA, however, it significantly decreased 6 to 12 months after the RFCA (p<0.05) (panel A). Although the NYHA functional class was demonstrated to be significantly worse before the RFCA (panel B), the RFCA significantly improved the NYHA functional class as compared to that before the intervention (p<0.01).