Electrophysiological Properties of the Right Atrial Septum in Patients with Atrial Tachyarrhythmias

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Common-type atrial flutter (AFL) is a type of atrial tachyarrhythmia with counterclockwise rotation around the tricuspid annulus within the right atrium (RA). It was recently reported that the electrogram voltage reduction observed in the RA was involved in the development of AFL. However, the relationship between the low voltage areas and conduction velocity during AFL has not been fully described. In this study, patients with AFL (n = 17) and without AFL (n = 4) were examined using an electro-anatomical mapping system. The patients with AFL were divided into 2 groups; AFL group (n = 8) and coronary sinus ostium (CSO) group (n = 9). The AFL group was defined as exhibiting the maintenance of AFL and the CSO group sinus rhythm before the catheter ablation. The electrogram voltages of each area in the RA (septum, and posterior and lateral walls), conduction velocity during AFL and transverse and longitudinal conduction velocities were evaluated. In the septum, the mean electrogram voltage was significantly lower in the AFL and CSO groups than in the group without AFL. Moreover, the conduction velocity during AFL was significantly slower in the septum, and both the septal transverse and longitudinal conduction velocities were significantly slower in the AFL and CSO groups than in the group without AFL. In conclusion, these findings suggest that both the slower conduction velocities and lower voltage in the RA septum may be involved in the development of AFL. Thus, ablation of the RA septum may represent a therapeutic approach of AFL.

Atrial tachyarrhythmias are classified into paroxysmal supraventricular tachycardia (PSVT), atrial tachycardia (AT), atrial flutter, and atrial fibrillation. The common type atrial flutter (AFL) is an atrial tachyarrhythmia with a counterclockwise rotation around the tricuspid annulus within the right atrium (RA). The electrical circuit of AFL exists within the right atrium (RA) and is formed by the anatomical and functional conduction barriers consisting of the crista terminalis (CT), Eustachian valve/ridge, inferior vena cava (IVC), and tricuspid annulus (TA) (Cosio et al. 1996; Jonathan et al. 1996). In AFL, the electrical conduction proceeds in a lateral to septal direction along the isthmus between the IVC and TA, ascends up the septum, and descends down the free wall (Cosio et al. 1996). The electrocardiographic characteristics of AFL exhibit sawtooth...
waves with negative deflections in the inferior leads and positive deflections in lead V1, whereas AT is defined as having an electrocardiographic pattern with the P-waves separated by an isoelectric line (Milliez et al. 2002).

The CT has been identified as a functional barrier within the posterior RA during AFL, which has been proposed to be critical for the predisposition of AFL maintenance. However, it has recently been suggested that transverse conduction block at the CT is not always consistent in some kinds of AFL because the electrical conduction penetrates the CT during AFL in such cases (Cheng et al. 1999; Tai et al. 2002). Functional barriers have also been noted at the sinus venosa region, which is located in the posteromedial RA, and the Eustachian ridge, which is located near the inferior septal RA, during AFL, regardless of the presence or absence of conduction block in the CT (Chen et al. 2003a; Tai et al. 2004; Huang et al. 2006).

The isthmus between the IVC and TA has been reported to be the slow conduction zone of the AFL circuit (Fled et al. 1997). Therefore, achievement of complete electrical conduction block in the isthmus between the IVC and TA is a curative ablation technique in patients with AFL. Recently, it was suggested that two zones of slow conduction existed in the septal part of the isthmus between the IVC and TA and in the lateral wall of the AFL circuit (Hassankhani et al. 2003). Further, both the medial isthmus and inferior septal wall have been demonstrated to be areas of slow conduction (Chen et al. 2003a). However, there has been some controversy as to the exact location of the area of slow conduction within the AFL circuit. Furthermore, the mean unipolar electrogram voltage of the global RA using a non-contact mapping system is significantly decreased during AFL as compared with sinus rhythm and this reduction has been noted in the lower septum as well as the CT and isthmus between the IVC and TA (Lin et al. 2005). Therefore, the relationship between the low voltage areas and conduction velocity in the AFL circuits has not yet been described. Thus, in the present study, we tested our hypothesis that the low voltage area in the RA septum is related to the slow conduction velocity with resultant induction and maintenance of AFL. For this purpose, we examined the electrogram voltage and conduction velocity of the RA in patients with AFL using an electro-anatomical mapping system.

**METHODS**

**Study population**

Twenty-one consecutive patients (17 men and 4 women; mean age: 61.1 ± 9.8 years) were examined in a retrospective review. The electrophysiological (EP) study and radiofrequency catheter ablation (RFCA) therapy were performed between September 2004 and May 2007. Out of the 21 patients, 17 had AFL (mean cycle length 223 ± 27 msec) with at least one ECG documentation of an AFL which was defined as having sawtooth waves with negative deflections in the inferior leads and positive deflections in lead V1 (Milliez et al. 2002). No AFL was documented in the remaining 4 patients, who underwent circumferential pulmonary vein isolation due to paroxysmal atrial fibrillation (PAF group, n = 4). Four patients (23%) had organic heart disease, including coronary artery disease in 2, a ventricular septal defect in 1, and dilated cardiomyopathy in 1 (Table 1).

The patients with AFL were divided into 2 groups; AFL group (n = 8) and coronary sinus ostium (CSO) group (n = 9). The AFL group was defined as exhibiting the maintenance of AFL and the CSO group sinus rhythm before the RFCA. However, no AFL could be induced in the CSO group in the EP study. In the AFL group, an examination of the electrical circuit using entrainment mapping during AFL was also performed to confirm that the atrial septum was part of the AFL circuit (Cosio et al. 1996). An examination in the RA using an electro-anatomical mapping system (CARTO, Biosense Webster, Inc., Diamond Bar, CA, USA) was performed during AFL in the AFL group and during electrical stimulation from the CSO at a cycle length of 600 msec (CSO pacing) after completion of bidirectional conduction block in the isthmus between the IVC and TA in the CSO and PAF groups. In the PAF group, no AFL was documented or could be induced in the EP study. Ablation of the isthmus between the IVC and TA was also performed in the PAF group in order to prevent any recurrence of PAF. Electrical conduction block in the isthmus between the IVC and TA was useful for excluding any electrophysiological influence of the RA septum on the clockwise electrical conduction through the isthmus between the
IVC and TA during CSO pacing. However, electrical conduction block in the isthmus between the IVC and TA could not be applied in the patients with any sustained atrial arrhythmias other than PAF.

**EP study and ablation procedure**

An EP study and RFCA were performed in all patients under informed written consent. All antiarrhythmic drug therapy was discontinued for at least 5 half-lives before the procedures, and no patients received any amiodarone. All patients were in a fasting state and mildly sedated with diazepam. A 5-F decapolar catheter was inserted via the right subclavian vein with its proximal electrodes placed at the CSO. Another venous access was obtained from the right femoral vein. A duodecapolar mapping catheter (Inquiry™, Irvine Biomedical Inc., Irvine, CA, USA) was positioned along the TA with its distal poles on the low lateral wall. A 5-F decapolar catheter was positioned in the His bundle region near the atroventricular node based on the His bundle electrograms. All catheters were deployed under fluoroscopy. The bipolar electrograms were filtered through a bandpass of 30-500 Hz, and the intracardiac electrograms and 12 lead surface ECGs were recorded with a computerized data acquisition system (CardioLab, GE Medical Systems, Milwaukee, WI, USA). The ablation of the isthmus between the IVC and TA was performed linearly from the ventricular side progressively to the IVC during either AFL or CSO pacing. Radiofrequency energy was delivered in a temperature-controlled mode with an upper temperature limit of 50°C, and maximal power output of 45W, using a quadrupolar 8-mm-tip electrode ablation catheter (Ablaze, Japan Lifeline, Tokyo) connected to a generator (CABL-IT, Japan Lifeline). In all 21 patients, bidirectional electrical conduction block of the isthmus was confirmed by differential pacing maneuvers after the ablation (Shah et al. 2000).

**Electro-anatomical three-dimensional mapping**

The electro-anatomical mapping system (CARTO, Biosense Webster, Inc., Diamond Bar, CA, USA) uses electromagnetic real-time technology to determine the location and orientation of the ablation catheter. By the induction of a low magnetic field generated by a location pad placed under the patient table and by the use of a catheter equipped with a passive location sensor, the precise catheter tip location can be determined. The mapping procedure is based on dragging the catheter along the endocardium and sequentially acquiring the location of the tip and local electrograms while in stable contact with the endocardium. The 3-D maps are constructed by combining and integrating the information from the intracardiac electrograms with the respective endocardial locations (Grothues et al. 2006).

A 3-dimensional geometry was constructed with the simultaneous display of a color-coded isochronal map on its surface (mean 179 ± 67 points/map). A reference of the activation time at each mapping site was set at the onset of the electrical activation sequence of the CSO in the mapping during AFL, and at the pacing stimulus in the mapping during CSO pacing.

**Conduction velocity in the RA**

The local electrical activation times were set and isochronal activation maps were created for each patient using the electro-anatomical mapping system. The conduction velocity (m/sec) was calculated as the ratio of the distance (m) between two points and the difference in the activation time (sec) between those two points. Based on the isochronal activation maps during typical AFL (5 msec between the isochrones), the conduction velocity was calculated in the major propagation direction in the superior and inferior septum, superior and inferior lateral free wall, posterior wall and lateral and medial isthmus, respectively.

Anisotropic electrical conduction properties may influence the conduction velocity. Therefore, the transverse and longitudinal conduction velocities of each area was measured in directions perpendicular and parallel to the superior and inferior vena cava line in the RA septum, free wall, and posterior wall in the electro-anatomical map, respectively. The conduction velocity (m/sec) was calculated as the ratio of the distance (m) between two points with at least a 5 mm distance in the transverse and longitudinal directions and the difference in the activation time (sec) between those two points. The software system determined the velocity contribution to the surface area of each point, presenting a probability density graph of the surface area according to the degree of the velocity. The mean conduction velocity in each area (RA septum, and lateral and posterior walls) was determined by the average of the conduction velocity among 10 pairs of points on the activation map during AFL and CSO pacing.

**Voltage mapping**

In the previous study, the mean bipolar and unipolar electrogram voltages were significantly lower in the
damaged myocardium than in the normal regions using the electro-anatomical mapping system (Fled et al. 1997). Therefore, in this study, we used the bipolar voltage maps and analyzed the peak-to-peak bipolar electrograms in the RA septum, posterior wall, and free wall during AFL and CSO pacing to evaluate the electrophysiological properties. The number of RF applications delivered to the isthmus between the IVC and TA for bidirectional electrical conduction block might not influence the RA septal voltage because the isthmus between the IVC and TA anatomically is located far from the RA septum.

**Statistical analysis**

Continuous data are expressed as the mean ± S.D. Statistical analyses were performed with StatView software (StatView 5.0, SAS Institute Inc., Cary, NC, USA). The mean values were compared using the Student’s unpaired t-test. The data were statistically analyzed using a one-way ANOVA and multiple comparison Scheffe test. A value of \( p < 0.05 \) was considered to be statistically significant.

**RESULTS**

**Patients population**

The study population consisted of the AFL group (\( n = 8 \), mean age: 61.0 ± 10.2 years, cycle length 237 ± 28 msec), CSO group (\( n = 9 \), mean age: 63.3 ± 11.0 years, cycle length 206 ± 14 msec), and PAF group (without any documentation of AFL and the inability to induce AFL in the EP study) (\( n = 4 \), mean age: 56.3 ± 5.1 years).

The RA mapping with the electro-anatomic system was performed during AFL in the AFL group and during pacing from the CSO at a cycle length of 600 msec after the ablation of the isthmus between the IVC and TA in the CSO and PAF groups. There was no significant difference among the groups in terms of the mean age, left atrial diameter, or left ventricular ejection fraction (Table 1).

**Voltage maps in the right atrium**

In the AFL group, the mean bipolar peak-to-peak electrogram voltage was significantly lower in the septal and posterior walls than in the lateral wall (1.35 ± 0.30 mV, 1.08 ± 0.26 mV vs 2.65 ± 0.53 mV, respectively, \( p < 0.001 \)), but no significant difference in the electrogram voltage was noted between the septal and posterior walls (1.35 ± 0.30 mV vs 1.08 ± 0.26 mV, respectively, NS) (Fig. 1A). Similarly, in the CSO group, the mean bipolar electrogram voltage was significantly lower in the septal and posterior walls than in the lateral wall (1.40 ± 0.45 mV, 1.31 ± 0.42 mV vs 2.90 ± 0.92 mV, respectively, \( p < 0.001 \)). However, there was no significant difference in the electrogram voltage noted between the septal and posterior walls (1.40 ± 0.45 mV vs 1.31 ± 0.42 mV, respectively, NS). In the PAF group, there was no significant difference in the mean bipolar electrogram voltage among the septal, posterior

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<th>Table 1. Clinical characteristics of the patients with AFL (AFL and CSO groups) and those without AFL (PAF group).</th>
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<tr>
<td><strong>AFL group</strong> (( n = 8 ))</td>
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LAD, left atrial diameter; LVFS, left ventricular fractional shortening; AFL, atrial flutter; CSO, coronary sinus ostium; PAF, paroxysmal atrial fibrillation.
Electrophysiological Properties of the Right Atrial Septum

The bipolar electrogram voltage mapping in the RA in the patients with typical AFL during AFL (A) and in those without AFL (PAF group) during electrical stimulation from the CSO at a cycle length of 600 msec (B). The mean bipolar electrogram voltages in the 3 different areas (the septal, lateral, and posterior walls) are shown. The results are shown as the mean ± s.d. *p < 0.001.

The mean bipolar electrogram voltage recorded from the RA septum in the 3 groups (the AFL, CSO, and PAF groups), respectively. The results are shown as the mean ± s.d. *p < 0.05.

and lateral walls (2.44 ± 1.22 mV vs 1.96 ± 0.82 mV vs 3.25 ± 1.01 mV, respectively, NS) (Fig. 1B). For the septal wall, the mean bipolar electrogram voltage was significantly lower in the AFL and CSO groups than in the PAF group (1.35 ± 0.30 mV, 1.40 ± 0.45 mV vs 2.44 ± 1.22 mV, respectively, p < 0.05) (Fig. 2).
Conduction velocity in the right atrium during AFL

The mean conduction velocity in the RA during AFL was significantly slower ($p < 0.05$) in the inferior (0.48 ± 0.16 m/sec) and superior (0.65 ± 0.29 m/sec) septum and the medial isthmus (0.46 ± 0.19 m/sec) than in the superior (1.19 ± 0.39 m/sec) lateral free wall, posterior wall (0.81 ± 0.17 m/sec) and lateral isthmus (0.87 ± 0.30 m/sec). There was no statistically significant difference in the conduction velocity among the inferior septum, superior septum and medial isthmus.

Transverse conduction velocity in the right atrium

In all 21 patients who underwent electro-anatomical mapping, the transverse conduction velocity was measured between 2 points with at least a 5 mm distance between. In the AFL group, the mean transverse conduction velocity was significantly slower in the septal and posterior walls than in the lateral wall (1.22 ± 0.34 m/sec, 0.49 ± 0.15 m/sec, vs 2.28 ± 0.58 m/sec, respectively, $p < 0.001$). Similarly, in the CSO group, the conduction velocity was more delayed in the septal and posterior walls than in the lateral wall (1.50 ± 0.42 m/sec, 0.78 ± 0.25 m/sec vs 2.47 ± 0.61 m/sec, respectively, $p < 0.001$). However, in the PAF group, the mean transverse conduction velocity was significantly slower only in the posterior wall than that in the septal and lateral walls (1.05 ± 0.24 m/sec vs 2.40 ± 0.38 m/sec, 2.07 ± 0.26 m/sec, respectively, $p < 0.001$). For the septal wall, the velocity was lower in the AFL and CSO groups than in the PAF group (1.22 ± 0.34 m/sec, 1.50 ± 0.42 m/sec vs 2.40 ± 0.38 m/sec, respectively, $p < 0.005$) (Fig. 3A and 4A).

Longitudinal conduction velocity in the right atrium

In the AFL group, the mean value of the lon-
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The longitudinal conduction velocity was significantly slower in the septum than that in the posterior and lateral walls (0.91 ± 0.23 m/sec vs 2.66 ± 0.66 m/sec, 2.31 ± 0.86 m/sec, respectively, \( p < 0.005 \)). In contrast, there was no significant difference in the longitudinal conduction velocity between the posterior and lateral walls. In the PAF group, there was no significant difference in the conduction velocity among the septal, posterior and lateral walls. Moreover, the longitudinal conduction velocity in the septum was significantly slower in the AFL and CSO groups than in the PAF group (0.91 ± 0.23 m/sec, 1.05 ± 0.24 m/sec, vs 2.09 ± 0.54 m/sec, respectively, \( p < 0.001 \)) (Figs. 3B and 4B).

**DISCUSSION**

In the present study, we were able to demonstrate the electrophysiological properties with regard to the voltage and conduction velocity of the RA in patients with AFL, using an electro-anatomical mapping system. Indeed, the patients with AFL were characterized by a lower mean bipolar voltage in the septum as compared with those without AFL. A conduction velocity delay in the septum was found during AFL. Moreover, both transverse and longitudinal conduction velocity delays were found only in the septum in the patients with AFL as compared to that in those without AFL. These findings indicate that both the slower conduction velocities and lower voltage in the RA septum may be involved in the development of AFL, which suggests ablation of the RA septum may be an effective strategy for the therapy of AFL.

**Voltage map in the right atrium**

Previous studies using an electro-anatomical mapping system (contact mapping) demonstrated that the reduction in the average bipolar electrogram voltage reflected abnormal myocardium (Gepstein et al. 1998; Kornowski et al. 1998), while non-contact mapping was also found to be useful for identifying those abnormalities (Lin et al. 2007). However, the electro-anatomical mapping may be superior to the non-contact mapping.
because the latter failed to accurately identify the areas of scar and low-voltage endocardium (Abrams et al. 2007). Thus, in the present study, we employed the electro-anatomical mapping system and examined the bipolar electrogram voltage in order to identify the electrophysiological properties of the RA. The reduction in the bipolar and unipolar electrogram voltages in the patients with a myocardial infarction could distinguish damaged myocardium from normal myocardium (Kornowski et al. 1998). Furthermore, previous studies using mapping with the bipolar electrogram voltage indicated that the areas of low voltage corresponded to the critical sites of reentrant ventricular tachycardia (Soejima et al. 2002; Hsia et al. 2003). However, even in patients with AFL without any structural heart disease, but not in those with atrial tachycardia with a focal origin or atrioventricular nodal reentrant tachycardia, the reduction in the bipolar and unipolar electrogram voltage was identified using the electro-anatomical system (de Groot et al. 2003). A recent study using a non-contact mapping system also demonstrated that the electrogram voltage was reduced in the RA septum as well as in the CT and isthmus between the IVC and TA during atrial pacing and AFL (Lin et al. 2005).

In the present study with the contact electro-anatomical mapping system, we were able to demonstrate, for the first time, that the mean electrogram bipolar voltage in patients with AFL was significantly lower in the septal and posterior walls than in the lateral wall not only during AFL but also during CSO pacing. However, in patients without documented AFL (PAF group), there was no significant difference in the mean bipolar electrogram voltage among all areas. For the septal and posterior walls, the mean bipolar electrogram voltage was significantly lower in the AFL group than in the PAF group. Taken together, these findings suggest that an increased fragmentation and fibrosis (Cosio et al. 1986) as identified by the reduction in the electrogram voltage in the RA septum and posterior wall, may contribute to the electrophysiological properties responsible for the slow conduction in patients with AFL.

**Conduction velocity in the right atrium**

The area of slow conduction in the atrial flutter circuit has been previously demonstrated to be the isthmus between the IVC and TA using the conventional catheter technique (Fled et al. 1997). However, the septal isthmus between the IVC and TA and lateral wall have been reported to be the slow conduction zones in the atrial flutter circuit using the non-contact mapping system (Chen et al. 2003b). In the present study, we noted that the conduction velocity during AFL was significantly lower in the septum, and that there were both transverse and longitudinal conduction delays in addition to the low voltage in the septum in the patients with AFL as compared with those without AFL. These findings suggest that such electrophysiological properties in the RA septum may be related to the inducibility and sustainability of AFL.

The wavefront of the electrical conduction in AFL has been reported to propagate up the RA septum in a caudocranial direction, down the lateral wall in a craniocaudal direction and transversely to the posterior wall (Cosio et al. 1996; Tai et al. 2004). However, the circuit remains to be fully identified. The present study demonstrated that, in the posterior wall, only the transverse conduction velocity was significantly slower in the patients with AFL. This suggests that the transverse conduction delay, especially that in the posterior wall, is related to the functional double block lines of the CT and sinus venosa regions (Chen et al. 2003a). However, it was demonstrated that a conduction gap in the CT exists in some kinds of AFL with a circuit around the lower RA or upper RA (Tai et al. 2002, 2004), and that the conduction through the TA- Eustachian ridge isthmus is also necessary in some kinds of AFL with a circuit around the lower RA (Cheng et al. 1999). Thus, various AFL circuits do not necessarily need the CT as posterior functional barriers.

**Mechanism of the electrophysiological properties in the right septum**

A previous study reported that the electrogram voltage distribution in the right atrium was functionally dependent on the cycle lengths (Lin
conduction velocity in the septum in the patients with AFL was found as compared to that in those without AFL even during CSO pacing at a cycle length of 600 msec after creating conduction block in the isthmus between the IVC and TA. Third, the electro-anatomical mapping system assumes a linear geometry and measures the distance between two points along a straight line despite the RA resembling a sphere, which may lead to an overestimation of the conduction velocity. Furthermore, the level of contact of the catheter on the tissue may be critical for obtaining the electrogram voltage on the contact map, so, this should be included as one of the limitations of this mapping technique. Finally, we examined a relatively small number of patients and the present findings remain to be confirmed in a future study with a larger number of patients.

**Conclusions**

We were able to demonstrate that in patients with AFL, the significant reduction in the bipolar electrogram voltage observed in the RA septum corresponds to the slow conduction velocity and anisotropic conduction areas. These findings indicate that both the slower conduction velocities and lower voltage in the RA septum may be involved in the development of AFL, which suggests ablation of the RA septum may be an effective strategy for the therapy of AFL.

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