High Atrial Defibrillation Threshold With Internal Cardioversion Indicates Arrhythmogenicity of Superior Vena Cava in Non-Long-Standing Persistent Atrial Fibrillation

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**Background:** The purpose of this study was to clarify the relation between atrial defibrillation threshold (ADFT) for internal cardioversion (IC) and arrhythmogenicity of the superior vena cava (SVC).

**Methods and Results:** A total of 159 consecutive patients (139 male, age 59.9±10.3 years) who underwent radiofrequency catheter ablation of atrial fibrillation (AF) were assessed. IC was performed in 50 patients with non-long-standing persistent AF (non-LSAF) with a purpose-built cardioversion catheter in which direct current is delivered between the right atrium and the coronary sinus. SVC arrhythmogenicity was defined as SVC firing initiating AF, SVC associated with maintenance of AF, or frequent ectopy in the SVC. In all 50 non-LSAF patients, AF termination was obtained on IC during the procedure except in 1 patient with SVC AF. In the patients with ADFT >10 J (n=10), SVC arrhythmogenicity was observed more often than in those with ADFT ≤10 J (n=40; 60% vs. 13%; P=0.004). There were no significant differences between the 2 groups in left atrial diameter (40.8±7.6 vs. 40.6±6.3 mm; P=0.92), persistent AF (33% vs. 50%; P=0.46), or other clinical parameters. The patients who underwent SVC isolation, however, had higher ADFT before SVC isolation than those who did not (15.5±8.8 vs. 9.2±4.4 J; P=0.01).

**Conclusions:** High IC ADFT is associated with SVC arrhythmogenicity in non-LSAF patients. (Circ J 2015; 79: 1479–1485)

**Key Words:** Atrial fibrillation; Catheter ablation; Defibrillation threshold; Internal cardioversion; Superior vena cava

External cardioversion (EC) is sometimes used for terminating drug-refractory atrial fibrillation (AF) and is recognized as a useful treatment option for it. Internal cardioversion (IC) is an alternative treatment that can be more effective and which delivers lower joule energy than EC. In some cases, especially in patients with long-episode AF or patients who have large left atrial (LA) diameter, multiple or high energy shocks are required to terminate AF, or worse, AF cannot be terminated at all. Past studies have shown a dependence of atrial defibrillation threshold (ADFT) on AF characteristics and atrial electrical substrate but there have been few studies on the relation between ADFT for IC and factors unrelated to atrial remodeling. We felt that it would be interesting to look for factors affecting ADFT for IC in patients in whom little atrial remodeling is expected, because we had encountered some AF patients with paradoxically high ADFT in spite of their small LA diameter. To this end, we investigated whether ADFT could be related to AF arising from or dependent on the superior vena cava (SVC) and which was not long-standing (non-LSAF), by which we mean paroxysmal AF or persistent AF. The SVC is a structure second only to the PV in importance for treating AF.
A total of 159 consecutive patients (139 men; mean age, 59.9±10.3 years; paroxysmal AF, n=112) who underwent PV isolation for AF at Medical Hospital of Tokyo Medical and Dental University between May 2012 and July 2013 were assessed. Of these patients, those who underwent IC and who did not have LSAF formed the study group. All patients gave written informed consent before the procedure. This study was approved by the institutional review board of Tokyo Medical and Dental University. AF was classified according to the HRS/EHRS/ECAS 2012 Consensus Statement on Catheter and Surgical Ablation of AF.

**Methods**

**Subjects**

A total of 159 consecutive patients (139 men; mean age, 59.9±10.3 years; paroxysmal AF, n=112) who underwent PV isolation for AF at Medical Hospital of Tokyo Medical and Dental University between May 2012 and July 2013 were assessed. Of these patients, those who underwent IC and who did not have LSAF formed the study group. All patients gave written informed consent before the procedure. This study was approved by the institutional review board of Tokyo Medical and Dental University. AF was classified according to the HRS/EHRS/ECAS 2012 Consensus Statement on Catheter and Surgical Ablation of AF.

**Ablation Procedure**

All anti-arrhythmic drugs were discontinued for at least 5 half-lives before the ablation, except in the LSAF patients, who were not part of the final study group.

All patients received >4 weeks of anticoagulation with warfarin or dabigatran before admission, and underwent transesophageal echocardiography 1 or 2 days before the procedure. Periprocedural anticoagulation was achieved with heparin at doses that maintained the activated clotting time >300 s. Analgesia was maintained with pentazocine.

At the start of the procedure, an IC catheter was advanced to the distal coronary sinus (CS) through the left subclavian vein, SVC, and right atrium (RA), and positioned to deliver effective IC (Figure 1). A decapolar electrode catheter was placed at the His bundle, apex of right ventricle, RA septum or tricuspid annulus as needed.

After the transseptal puncture, decapolar circular electrode catheters (Lasso, Biosense Webster, Diamond Bar, CA, USA) and an irrigation catheter (Thermo-cool, Biosense Webster) were advanced into the LA through the long SL0 sheaths (St. Jude Medical, Minneapolis, MN, USA).

Before starting radiofrequency (RF) application, isoproterenol and adenosine triphosphate (ATP) were infused to determine whether AF was induced and where. Bilateral PV isolation was accomplished with the double LASSO technique for all patients, utilizing 3-D electro-anatomical mapping (CARTOXP or CARTO3; Biosense Webster).

If needed, ablation for the cavitricuspid isthmus (CTI) was performed. After completion of PV isolation and CTI ablation, we checked for dormant PV-LA conduction, AF inducibility and non-PV foci using isoproterenol infusion, ATP infusion, and CS burst pacing. If AF could not be terminated by IC and/or EC, or sustained AF was induced by CS pacing, we also performed electrogram-based ablation and/or linear ablation such as roofline, bottom line, and mitral isthmus line ablation.

When the SVC appeared to be involved in AF, SVC isolation was also performed. When non-PV ectopies initiating AF other than SVC were detected during the procedure, these foci were eliminated to the fullest extent possible.

**IC Protocol**

Before PV isolation, if AF persisted at baseline or was induced by the aforementioned induction maneuver, IC was used first to terminate AF. We used the Bee AT (Japan Lifeline, Tokyo, Japan) catheter and dedicated defibrillator (Shock AT, Japan Lifeline) which together constitute the only IC system currently approved for use in Japan.

The Bee AT catheter has 20 poles consisting of a distal set of 8 poles, a middle set of 8 poles and a proximal set of 4 poles. The distal 8 poles are positioned in the distal CS and the middle 8 poles at the lateral wall of the RA. Cardioversion is effected by current delivery between these distal and middle sets of electrodes, but they are also able to record local electrograms. The proximal 4 poles are positioned in the SVC and record SVC activity during the procedure. For cardioversion, a biphasic direct current is delivered between the distal set and the middle set of electrodes synchronized to the R wave of the body surface electrocardiogram. The maximum energy output is 30 J in this system. The electrodes for current delivery are 4 mm long with 2-mm inter-electrode spacing. The pulse duration ratio of the biphasic wave is fixed at 6:4 and the pulse duration is adjusted automatically based on the resistance.

IC was performed under anesthesia with thiopental sodium. We started the IC at 5 or 10 J and increased it in steps of 5 J until AF was terminated. We regarded AF as terminated even when AF recurred immediately after cardioversion.

**SVC Arrhythmogenicity and SVC Isolation**

As described in the ablation procedure section, we tested SVC arrhythmogenicity before and after PV isolation with drug challenges and pacing maneuvers. In the present study, arrhythmogenic SVC was defined as occurrence of any of the following phenomena during the procedure: (1) electrogram activity in the SVC initiating AF; (2) frequent ectopy from the SVC after complete electrical PV isolation; (3) AF in SVC with passively excited atrium (SVC associated with the maintenance of AF).
Figure 2. Representative case of paroxysmal atrial fibrillation (AF) with arrhythmogenic superior vena cava (SVC) associated with maintenance of AF, in which the atrial defibrillation threshold was >30 J, and the length of the SVC sleeve was 58 mm. AF was initiated by catheter manipulation and was sustained. (A) At the beginning of the session, internal cardioversion (IC) with an output energy of 30 J (red arrow) failed to restore sinus rhythm. Note that the excitation recorded by the proximal electrodes of the multi-electrode catheter for IC located at SVC was not interrupted by IC, although excitation in the left atrium (LA) and right atrium (RA) were slightly affected and organized by IC. (B) After completion of bilateral pulmonary vein (PV) isolation, the AF cycle length was significantly prolonged in LA and RA, but not in SVC. In SVC, rapid activity was still observed, and there was a significant gradient in the tachycardia cycle length between SVC and RA. (C) After electrical SVC isolation, local electrograms in LA, RA and body surface electrocardiogram showed sinus rhythm, although AF still persisted in the SVC. CS, coronary sinus; d, distal; p, proximal.
The length of the SVC sleeve was measured in patients with arrhythmogenic SVC in a fashion similar to that in a previous report. Briefly, the SVC sleeve was defined as the segment of SVC in which SVC potentials could be recorded, and the proximal limit of the SVC sleeve (electrical SVC-RA junction) was determined to be where merged SVC and local RA potentials were present. The proximal and distal limits of the sleeve were determined using the circular mapping catheter, after which the length between them was measured utilizing 3-D electro-anatomical mapping.

SVC isolation was performed only if SVC arrhythmogenicity as defined was observed during the procedure. SVC isolation was performed at the level of the RA-SVC junction guided by SVC venography and 3-D electro-anatomical mapping. During this procedure, we confirmed that pacing from the tip of the ablation catheter did not capture the phrenic nerve just before starting RF application, in order to minimize damage to the phrenic nerve. The endpoint of the procedure was the complete elimination of SVC potentials recorded on the electrodes of the circular mapping catheter placed inside the SVC.

**Statistical Analysis**

Continuous data are given as mean ± SD, and were compared using Student’s t-test or Mann-Whitney U-test as appropriate. Categorical variables were compared using chi-squared test or Fisher’s exact test as appropriate. Statistical analysis was performed using JMP version 10 (SAS Institute, Cary, NC, USA). P<0.05 was considered statistically significant.

**Results**

**Patient Characteristics**

Of the 159 patients, IC was attempted in 69 patients (43%); in the remaining 90 patients, IC was not performed because sustained AF, for which IC was applicable, could not be induced. The IC catheter was able to be placed in an appropriate position and IC performed in 67 patients, 17 of whom were LSAF patients and 50 of whom were not. There were 2 patients (3%) requiring cardioversion in whom the IC catheter could not be positioned as required and who had to be cardioverted using EC.

In the 50 non-LSAF patients who underwent IC during the procedure (44 men; persistent AF, n=18), AF termination was obtained by IC with output energy ≤10 J except in 1 patient in whom AF was not terminated by the maximum IC energy of 30 J. We set this patient’s ADFT as 30 J in the analysis (Figure 2).

Of the 50 patients, 11 non-LSAF patients (22%) received SVC isolation because of SVC firing initiating AF (n=4), frequent ectopy from the SVC after complete electrical PV isolation (n=4), and SVC associated with the maintenance of AF (n=4), with 1 patient overlapping in the first and third categories.

SVC isolation was successful in all, and no adverse event related to IC and SVC isolation was observed in this study, except for diaphragmatic paralysis after the procedure in 1 patient, which did not require specific treatment. Clinical and procedural characteristics are listed in Table 1.

**ADFT and Clinical and Procedural Parameters**

The patients with ADFT ≤10 J (n=10) underwent SVC isolation more frequently than those with ADFT >10 J (n=40; P=0.004; 60% vs. 13%). There were no significant differences between the 2 groups in LA diameter (40.8±7.6 mm vs. 40.6±6.3 mm, P=0.92), prevalence of persistent AF (33% vs. 50%, P=0.46), body mass index (BMI; 24.8±4.0 vs. 25.6±3.7, P=0.55), or other clinical parameters. The starting IC energy was similar (7.6±2.5 J vs. 8.0±2.6 J) in the 2 groups, whereas the number of attempted IC was significantly greater in the patients with ADFT >10 J than in those with ADFT ≤10 J (3.2±1.0 times vs. 1.1±0.3 times). AF duration of persistent AF was 7.5±2.9 months in the patients with ADFT >10 J, and 9.4±2.9 months in those with ADFT ≤10 J (P=0.20). There were 6 patients with pulmonary disease (1 sleep apnea syndrome [SAS], and 1 past history of pulmonary tuberculosis [TB] in the patients with ADFT >10 J, vs. 2 SAS, 1 past history of pulmonary TB, and 1 pulmonary sarcoidosis in the patients with ADFT ≤10 J; 20% vs. 10%, P=0.59).

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**Table 1. Subject Clinical Characteristics**

<table>
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<tr>
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<th>ADFT ≤10 J</th>
<th>ADFT &gt;10 J</th>
<th>P-value</th>
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<tr>
<td>No. patients</td>
<td>40</td>
<td>10</td>
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<td>Age (years)</td>
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<td>Male</td>
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<td>Body weight (kg)</td>
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<td>BMI (kg/m²)</td>
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<td>Structural heart disease</td>
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<td>Pulmonary disease</td>
<td>4 (10)</td>
<td>2 (20)</td>
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<td>Persistent AF</td>
<td>13 (33)</td>
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<td>LA diameter (mm)</td>
<td>40.8±7.6</td>
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<td>Ejection fraction (%)</td>
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<td>Initial IC energy (J)</td>
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<td>SVC arrhythmogenicity</td>
<td>5 (13)</td>
<td>6 (60)</td>
<td>0.004</td>
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</table>

Data given as mean ± SD or n (%). ADFT, atrial defibrillation threshold; AF, atrial fibrillation; BMI, body mass index; IC, internal cardioversion; LA, left atrium; PAF, persistent atrial fibrillation; SVC, superior vena cava.
The patients who underwent SVC isolation had significantly higher ADFT than those who did not (15.5±8.8 J vs. 9.2±4.4 J, P=0.01; Table 2). Otherwise, the presence of arrhythmogenic SVC was not affected by AF type, LA diameter, BMI, the presence of pulmonary disease or other parameters. There was no significant difference in initial attempted IC energy between the patients with or without arrhythmogenic SVC. The mean length of the arrhythmogenic SVC sleeve was 32.9±13.5 mm (range, 22–58 mm).

**Discussion**

**SVC Arrhythmogenicity and ADFT**

To our knowledge, this is the first report to systematically...
show a relation between SVC arrhythmogenicity and ADFT with IC in non-LSAF patients. The SVC is well-known as an important structure when treating AF with ablation, because it is the most frequent source of arrhythmogenic foci after the PV.\textsuperscript{20,21} The SVC also plays an important role in maintenance of AF (Figure 2).\textsuperscript{11} Therefore, locating arrhythmogenic SVC and performing SVC isolation is critical in treating AF.\textsuperscript{22,23}

Miyazaki et al suggested the possibility of an association between high ADFT and arrhythmogenic SVC in a similar IC system.\textsuperscript{11} The cause of this phenomenon could be the catheter configuration in this unique IC system, in which direct current is delivered between the 2 sets of electrodes in the RA and CS, and does not include the SVC in its field (Figure 3). This system could be inadequate in depolarizing the cardiac muscle of the long SVC sleeve, which is not flanked by the electrodes of the IC, due to insufficient current reaching the SVC. Thus, higher ADFT could indicate a longer SVC sleeve, in which AF can persist even while IC is performed.

We previously reported an association of long SVC sleeve with arrhythmogenic SVC as a source of AF triggers.\textsuperscript{24} We speculate that some SVC with long sleeve can serve not only to trigger but also to maintain AF, just as the PV and antrum can. Therefore, high ADFT under IC may be a feature of patients with arrhythmogenic SVC, with long sleeve working as an AF trigger and/or AF maintenance. In fact, the length of the arrhythmogenic SVC sleeve in the present study (32.9±13.5 mm) would be categorized as long according to the previous study, in which the length of SVC sleeve in arrhythmogenic SVC was 34.7±4.4 mm, whereas that in non-arrhythmogenic SVC was 16.5±11.4 mm.\textsuperscript{24}

Other Factors Related to ADFT With IC
In previous studies, ADFT has been shown to be related to clinical parameters such as AF type, duration, and LA diameter, suggesting an association between ADFT and the extent of atrial remodeling.\textsuperscript{10,14,15} In the present study, we excluded patients with LSAF from the analysis, to better isolate factors affecting ADFT independent of remodeling. Perhaps due to this design, no significant difference was found in clinical characteristics including LA diameter and AF duration between low ADFT and higher ADFT patients.

SVC Isolation and Definition of Arrhythmogenic SVC
The prevalence of arrhythmogenic SVC (11/50) was greater in this study compared with past studies (5–12%).\textsuperscript{11,20,21,23} This may be because we did not limit the definition of arrhythmogenic SVC to SVC triggers of AF (4/50). A representative case of SVC associated with AF maintenance is given in Figure 2, in which SVC firing initiating AF was not observed, possibly because SVC firing was masked by sustained AF before PV isolation, or because the SVC was necessary purely for AF maintenance.

We also defined SVC with frequent ectopy after PV isolation as arrhythmogenic SVC, because it is possible that SVC firing was masked by PV firing and/or sustained AF, or that it happened not to be inducible by isoproterenol infusion and pacing maneuver before PV isolation.\textsuperscript{25} The possibility that such SVC firing had been an important trigger before the removal of the maintenance source in PV by RF catheter ablation could not be ruled out. Although the clinical significance of isolating the SVC in cases in which the SVC displays frequent ectopy after PV isolation and does not appear to trigger AF directly, is undetermined, we believe such an SVC has arrhythmogenic potential.

Clinical Implications
The usefulness of the conventional assessment of SVC arrhythmogenicity with pacing maneuver and isoproterenol infusion is well-established. Conventional assessment, however, is not sufficient for identifying candidates for SVC isolation.\textsuperscript{26} For example, some patients, in whom SVC arrhythmogenicity had not been seen on conventional assessment in the first session, are found to need SVC isolation in a later ablation session in which SVC arrhythmogenicity is identified on the same conventional SVC assessment as in the first session.\textsuperscript{27} To reduce such avoidable repeat ablation sessions for AF patients, additional complementary approaches for identifying SVC arrhythmogenicity would be highly useful.

Furthermore, this IC maneuver may have an advantage in identifying arrhythmogenic SVC associated with the maintenance of AF (Figure 2).\textsuperscript{11} We therefore believe that, in this respect, this IC maneuver has potential as an addition to conventional approaches for identifying SVC triggers.

Based on the present results, we believe a precise assessment of SVC arrhythmogenicity should be considered when multiple and high-energy IC unexpectedly fails to restore sinus rhythm during AF ablation in non-LSAF patients. IC using 2 sets of multi-electrodes at the CS and RA could be a novel maneuver for assessing the presence of SVC arrhythmogenicity.

Study Limitations
This study has some important limitations. First, this was a retrospective study with a small sample size, not a prospective randomized study. A randomized study with a larger study population is needed to clarify the true involvement of SVC arrhythmogenicity in ADFT with IC. Second, in the present IC protocol, the starting IC energy was determined by the operator. In the patients in whom IC was started at 10 J and the 10 J was sufficient to cardiovert, ADFT may have been overestimated compared with the patients in whom IC was started at 5 J. The patients with arrhythmogenic SVC, however, had higher ADFT and a higher number of IC (1.2±0.7 vs. 2.4±1.2, P=0.003), although there was no significant difference in initial attempted IC energy between the patients with or without arrhythmogenic SVC (7.8±2.5 J vs. 7.2±2.6 J, P=0.52; Table 2). This indicates that this IC protocol had little effect on the main findings in this study. Third, a purpose-built IC catheter was used in this study, but its configuration of electrodes for IC was similar to that in previous reports.\textsuperscript{3–5,10} and we surmise that ADFT with other IC techniques using the same configuration would also be associated with SVC arrhythmogenicity, considering its aforementioned putative mechanism. Fourth, the length of SVC sleeve was not measured in all subjects; it was measured only in the patients undergoing SVC isolation. Therefore, we were unable to compare SVC sleeve length between the patients with SVC isolation and those without it. Based on a previous study, however, it is likely that the present patients who underwent SVC isolation had relatively longer SVC sleeve.\textsuperscript{29}

Conclusions
The ADFT for IC of non-LSAF in patients with arrhythmogenic SVC is high, possibly because the SVC does not lie between the 2 sets of the internal cardioverter electrodes when they are placed in the configuration of the BeeAT IC system, and other similar systems.

References
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