Initiation of Atrial Fibrillation by Ectopic Beats Originating From the Superior Vena Cava

Electrophysiological Characteristics and Results of Radiofrequency Ablation

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Background—The superior vena cava (SVC) has cardiac musculature extending from the right atrium. However, no previous study in humans has given details regarding the ectopic foci that initiate paroxysmal atrial fibrillation (PAF), which may originate from the SVC.

Methods and Results—A total of 130 patients with frequent attacks of PAF initiated by ectopic beats were included. Eight patients (6%) had spontaneous AF initiated by a burst of rapid ectopic beats from the SVC (located 19±7 mm above the junction of the SVC and right atrium), which was confirmed by multiplane angiographic and intracardiac echocardiographic visualization and was marked by a sharp SVC potential preceding atrial activity. During initial repetitive discharges, the group with SVC ectopy had a higher incidence of intravenous conduction block than the group with pulmonary vein ectopy (75% versus 37%; P=0.03). The activation time of the earliest intracardiac ectopic activities relative to ectopic P wave onset was significantly shorter in the SVC ectopy than the pulmonary vein ectopy group (37±15 versus 84±32 ms; P<0.001). After 5±3 applications of radiofrequency energy, AF was eliminated. SVC angiography after ablation revealed a local indentation of the venous wall in one patient. Two patients manifested coexisting sinus rhythm and a “focal” fibrillating activity confined inside the SVC after radiofrequency ablation. During a follow-up period of 9±3 months, all 8 patients were free of antiarrhythmic drugs, without tachycardia recurrence or symptoms of SVC obstruction.

Conclusions—Ectopic beats initiating PAF can originate from the SVC. A radiofrequency current delivered to eliminate these ectopies is a highly effective and safe way to prevent PAF. (Circulation. 2000;102:67-74.)

Key Words: catheter ablation □ fibrillation □ vena cava, superior

Atrial fibrillation (AF) is thought to be perpetuated by multiple reentrant wavelets in both atria. The focal mechanisms of AF were suggested by some mapping data, and they were proved by radiofrequency ablation.2–7 The pulmonary veins (PVs) were recently demonstrated to be the major sites of the ectopic foci initiating paroxysmal AF (PAF); an extension of atrial muscle into the PVs with abnormal automaticity might be the underlying mechanism.8–16 However, only limited data are available on PAF originating from the superior vena cava (SVC) in humans.12–14,17–20

Therefore, this study was conducted to (1) investigate the electrophysiological features and results of radiofrequency ablation in patients with spontaneous AF initiated by ectopic beats originating in the SVC and (2) compare the characteristics of ectopic foci originating in either the SVC or PVs.

Methods

Study Patients
A total of 130 patients with clinically documented attacks of PAF were included in the study. Their 24-hour Holter recordings showed frequent atrial premature beats and runs of atrial tachycardia or AF (6±4 episodes/day) preceded by repetitive atrial beats. The patients were refractory to or intolerant of 3±1 antiarrhythmic drugs. As described previously, all antiarrhythmic drugs except amiodarone were discontinued for ≥5 half-lives before the study.7–11

Catheter Positions
As described previously, mapping of the superior PVs was guided by selective PV angiography, with the first pair of electrodes straddling...
Radiofrequency Catheter Ablation

As described previously, the presumed ablation site showed the earliest bipolar ectopic activities preceding AF as recorded from the PVs, SVC, or atrial wall.7–11 The successful ablation site in the SVC (8 patients) was confirmed by SVC angiography and/or intracardiac echocardiography. The ablation catheter (4-mm tip electrode, Mansfield, Boston Scientific) was connected to an EPT-1000 generator (EP Technologies) that delivered a 550-kHz sine wave output between the distal electrode of the ablation catheter and the cutaneous patch electrode placed over the left scapula.

Temperature-controlled (target temperature, 60°C) radiofrequency energy was delivered for 40 s/pulse, but it was terminated immediately if the ablation catheter displaced or if the patient complained of burning pain, coughed, or developed severe bradycardia.10 Thereafter, we also decreased the maximal temperature to 50°C to 55°C during the following energy applications. The ablation end point was total elimination or marked reduction (∼50% of the initial amplitude) of ectopic focus amplitude. The protocols used to facilitate PAF initiation before ablation were repeated twice to assess the effects of radiofrequency ablation immediately after and 30 minutes after the last energy application.

Postablation Follow-Up

Close clinical follow-up visits (2 weeks, 1 month, and then every 2 months) consisted of 24-hour Holter recordings at 1 to 6 months after ablation. If patients experienced palpitation, another 24-hour Holter monitoring or recording of cardiac events was performed to define the cause of tachycardia. Long-term follow-up information was also obtained from all patients by the referring physicians and through telephone interviews with the patients.

Statistical Analysis

Parametric data were presented as means±1SD, and they were analyzed by a paired Student’s t test or by ANOVA, as appropriate.

Electrophysiological Study

As described previously, each patient underwent the electrophysiological study in a fasting, nonsedated state after informed consent was obtained.7–9 Because these patients had clinically documented spontaneous onset of PAF, we tried to find spontaneous ectopic beats initiating AF before or after the infusion of isoproterenol or after the previously designed algorithm used for facilitating the initiation of AF.11 If a consistent ectopic focus and onset pattern of spontaneous AF was confirmed, the earliest ectopic site was considered to be the initiating focus of AF. The methods used to facilitate spontaneous AF were tried at least twice to ensure reproducibility.

Electrographically, we determined the region of earliest activation in sinus rhythm that was characterized by the initial negative rapid deflection and/or fusion of the major atrial electrogram and the SVC muscular potential.13,14 Additionally, intracardiac ultrasound imaging (10 French/10-MHz catheter, Boston Scientific Co and CVIS, Inc) was used to delineate the atrio caval junction area in comparison with angiographic localization. In some patients with typical atrial flutter, a 7 French, 20-pole, deflectable “halo” catheter with 10 mm paired spacing (Cordis-Webster Inc) was positioned around the tricuspid annulus for simultaneous mapping.

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Statistical Analysis

Parametric data were presented as means±1SD, and they were analyzed by a paired Student’s t test or by ANOVA, as appropriate.
Nonparametric data were analyzed by the $\chi^2$ test with Yates’ correction or Fisher’s exact test. \( P \leq 0.05 \) was considered statistically significant.

**Results**

**PAF Initiated by SVC Ectopy**

**Patient Population**

All 130 patients had spontaneous AF paroxysms originating from ectopic foci. Eight patients (6%; 4 men and 4 women; mean age, 55±12 years; range, 35 to 74 years) had a spontaneous initiation of PAF by ectopic beats originating from the SVC (posterior wall in 6 and anterior wall of SVC in 2). They were refractory to treatment with 2.8±0.7 antiarrhythmic drugs (Table 1).

**SVC Activity During Sinus Rhythm and Ectopy**

During sinus rhythm, the SVC potentials with a rapid deflection (duration, <50 ms; amplitude, >0.05 mV) were recognized along the SVC in a proximal-to-distal venous activation sequence to a height of 33±7 mm (range, 24 to 44 mm) above the junction of the SVC, with a base at the right atrial appendage (Figures 1 and 2A). The SVC potential was fused with the local atrial electrogram at the ostium; it was separated from far-field right atrial activity and occurred progressively later toward the distal SVC.

The earliest ectopic activity in the SVC exhibited temporal reversal with far-field right atrial activity and proceeded toward the right atrial entrance, resulting in a distal-to-proximal SVC activation sequence. In contrast,
the PV potentials recorded in both superior PVs showed the same sequence and relationship with atrial activity as those during sinus rhythm (Figure 2A).

**Spontaneous Initiation of AF**

The methods used to provoke spontaneous AF included an isoproterenol infusion (1 patient), short-duration burst pacing with an isoproterenol infusion (2 patients), and cardioversion after electrical induction of sustained AF, with or without isoproterenol infusion (4 patients). The last patient had a spontaneous onset of AF in the baseline state. The earliest local electrogram during the spontaneous onset of AF was recorded at the same site as SVC ectopy. During the initial seconds of repetitive depolarization of ectopic foci and/or during self-perpetuating AF confined in the SVC, 6 patients (75%) showed a Wenckebach or 2:1 conduction pattern inside the SVC or near the sinocaval junction (Figure 2B).

The earliest ectopic activity that conducted to the right atrium preceded the onset of the ectopic P wave by a mean of 37±15 ms (range, 10 to 90 ms).

**Effect of Radiofrequency Ablation**

After 5±3 applications of radiofrequency energy (range, 3 to 13 applications), 6 of 8 SVC ectopic foci were completely eliminated; the other 2 ectopic foci were partially eliminated, as indicated by the presence of only premature atrial ectopy that did not initiate AF. The successful ablation site could be traced to a point 19±7 mm (range, 10 to 28 mm) above the SVC–right atrial junction. Right shoulder pain in one patient and chest discomfort in 2 patients occurred during the ablation procedure.

Shortly after ablation, SVC angiography showed an indentation of the venous wall at the ablation site in one patient, and his intracardiac echocardiogram revealed focal tissue swelling (edema) causing focal narrowing; venograms were unremarkable in other patients. After ablation, only anxiolytics and low-dose propranolol (10 mg BID to TID) were prescribed intermittently for mildly symptomatologic premature atrial beats. Patients 3 and 8 only took anxiolytics and low-dose propranolol (10 mg BID to 156±12 ms, respectively. This occurred by the fifth to sixth cycle of the tachycardia, with ectopic firing continuing or degenerating into continuous or fragmented electrical activity. The coupling intervals from the last sinus beat to the first ectopic beat were similar between SVC and PV foci, but the coupling interval from the onset of local intracardiac ectopic activity to the onset of the surface ECG ectopic P wave was significantly shorter in SVC ectopy than PV ectopy (37±15 versus 84±32 ms; P<0.001). However, the provocative maneuvers used to facilitate the onset of PAF were similar between the 2 groups. The incidence of intra-PV conduction block during the spontaneous onset of AF paroxysms was significantly less than the intra-SVC conduction block (30% versus 75%; P=0.03).

The immediate success rates of radiofrequency ablation were similar in both groups; however, patients with PAF initiated by PV ectopy had a higher recurrence rate of AF during the follow-up period (Table 2).

**Comparison of the Ectopy of the SVC and PVs**

In comparison with the SVC ectopy, almost half of the PV foci initiated spontaneous AF by a rapid run (>3) of ectopic beats. AF of either SVC or PV origin was initiated by a short burst of ≥3 repetitive focal discharges, which progressively shortened the tachycardia cycle length to 171±13 and 156±12 ms, respectively. This occurred by the fifth to sixth cycle of the tachycardia, with ectopic firing continuing or degenerating into continuous or fragmented electrical activity. The coupling intervals from the last sinus beat to the first ectopic beat were similar between SVC and PV foci, but the coupling interval from the onset of local intracardiac ectopic activity to the onset of the surface ECG ectopic P wave was significantly shorter in SVC ectopy than PV ectopy (37±15 versus 84±32 ms; P<0.001). However, the provocative maneuvers used to facilitate the onset of PAF were similar between the 2 groups. The incidence of intra-PV conduction block during the spontaneous onset of AF paroxysms was significantly less than the intra-SVC conduction block (30% versus 75%; P=0.03).

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**Discussion**

**Electrically Active Cardiac Muscle in the SVC**

The present study recorded the SVC potentials around the SVC orifice and the myocardial sleeve inside the SVC;
presumably, these potentials represent the depolarization of cardiac myocytes in the SVC. The mean distances determined by the electrical measurement in this study (33±7 mm; range, 24 to 44 mm) were comparable to those of previous studies. Histological findings showed atrial muscle extensions in these veins, with a 2 to 5 cm distance above the atrium.

**Focal PAF Initiated by SVC Ectopy**

The proximal SVC in the adult mammalian heart is thought to originate from the embryonic sinus venosus (right sinus horn). Considering that the embryological sinus precursor encompasses all of the pacemaker sites, cardiac muscle in the SVC is likely to have ectopic pacemaker activity. The present study suggests that the possible mechanisms might be abnormal automaticity or triggered activity. Ito et al. showed phase 4 depolarization accompanied by the initiation of automatic activity in the SVC. Moreover, Yanaga reported abnormal automaticity and fibrillation induced by aconitine in the musculature of the SVC. Therefore, the atrial muscle extension into the SVC could be the source of the spontaneous ectopy recorded in the SVC.

**“Focal Source” and “Pseudosinus Rhythm”: Implicating the Ablation Lesions in the Great Thoracic Veins**

The present study delineated the focal source of AF inside the SVC by the findings that focal ablation terminated AF and/or prevented AF reinduction. Termination of AF during the
delivery of radiofrequency energy at the SVC ectopic focus indicated that the ectopic focus contributed to both the initiation and maintenance of AF.

In this study, the coexistence of normal sinus activity and fibrillating activity confined in the SVC also provided direct evidence of a focal mechanism of AF. The surface ECG showed normal sinus P waves, regardless of the presence of rapid fibrillation activity in the SVC. In an early experimental study of aconitine-induced focal AF in the atrial appendage, Moe and Abildskov\textsuperscript{24} demonstrated the coexistence of sinus rhythm and atrial tachycardia/AF. After clamping the atrial appendage, AF ceased in the atria but atrial tachycardia or AF remained in the atrial appendage. In our cases, the dissociated sinus rhythm was most likely related to the exit block of venous ectopic activity by the focal delivery of radiofrequency energy at a critical conduit of conducting atrial myocardium extending into the SVC.

Previous reports have demonstrated the coexistence of different atrial arrhythmias resulting from intraatrial or interatrial conduction block.\textsuperscript{14,25} Kirchhof and Allessie\textsuperscript{26} demonstrated a high degree of dissociated activation of the sinus node during AF with their recordings of continuous concealed sinus automaticity with a high degree of sinoatrial entrance and exit block. Ito et al\textsuperscript{17} also showed an example of atrio caval dissociation by their recordings of isolated ectopic pacemaker activity in the left-sided caval veins without AF in the rabbit preparation, and they proposed that delay or block sites were located in a slow conduction zone near the sinocaval junction area.

Furthermore, there is still some controversy regarding the definition and true incidence of focal AF in AF paroxysms. Previous studies and this report demonstrated that similar, but not identical, electrophysiological findings can yield the same ECG characteristics, namely AF. However, in some cases, venous ectopic activity presenting as single beats or bursts of rapid firing induced AF (focal-initiated AF); in the other cases, continuously firing foci initiated and maintained AF (focally initiated and maintained AF).\textsuperscript{6–11}

Radiofrequency Ablation of PAF Originating From the SVC

Although the present study demonstrated that the application of radiofrequency energy in the SVC was feasible and safe, a recent study raised concerns about the risk of atrial swelling, with resultant critical narrowing at venous ostia due to multiple radiofrequency current applications at the upper crista region for the ablative therapy of inappropriate sinus tachycardia.\textsuperscript{27} In this study, we used a smaller ablation tip electrode (4 versus 8 mm), fewer radiofrequency applications (5–6 versus 29–620 pulses), and a shorter pulse duration (40 versus 120 s) than did Callans et al.\textsuperscript{27} We had no immediate or late complications.

The present study had a higher success rate and a lower recurrence rate than the results of focal ablation at the PVs.\textsuperscript{8,9} The true incidence of recurrent AF after initially successful ablation is uncertain because the attacks of AF were paroxysmal in our patients and it is difficult to detect asymptomatic AF by a noninvasive follow-up method. Thus, the true results of catheter ablation should be interpreted carefully. However, in all patients, antiarrhythmic medication could be discontinued after ablation, and all patients were free of arrhythmic
symptoms. Therefore, the natural history of PAF originating from the different great thoracic veins may require a longer follow-up period by using more comprehensive follow-up tools, ie, loop recorders, teletransmission ECG, or follow-up electrophysiological study.

Study Limitations
We did not routinely map the SVC for the first 34 patients; thus, it is possible that we missed some patients with ectopic activity originating in the SVC. However, no earliest ectopic activity was recorded from the high crista or atroioval region among these patients. The success of ablation could be due to the elimination of other potential mechanisms of AF, ie, autonomic nerve innervation or the local blood supply of the myocardial sleeve. However, the amplitude of ectopic activity was closely related to the feasibility of the reinitiation of AF. Thus, the elimination of ectopic foci activity is the major cause of the successful procedure.

Conclusions
SVC can be a focal source of atrial ectopy initiating PAF. The application of radiofrequency energy in the SVC is a highly effective and safe methods for the ablation of venous ectopies and is a cure of this type of PAF. Curative ablation therapy for PAF can be achieved by applying radiofrequency energy to the atroioval junction or inside the SVC.

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References

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<thead>
<tr>
<th>TABLE 2. Comparison of Ectopy Features Between the SVC and PVs</th>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>No. of Patients</td>
</tr>
<tr>
<td>AF onset</td>
</tr>
<tr>
<td>Spontaneous isoproterenol</td>
</tr>
<tr>
<td>Pacemaker isoproterenol</td>
</tr>
<tr>
<td>Postcircumferential isoproterenol</td>
</tr>
<tr>
<td>Initiated by burst of rapid ectopic beats</td>
</tr>
<tr>
<td>Coupling interval to the last sinus beat, ms</td>
</tr>
<tr>
<td>Interval preceding ectopic P wave, ms</td>
</tr>
<tr>
<td>Intravenous conduction block during AF</td>
</tr>
<tr>
<td>Radiofrequency ablation</td>
</tr>
<tr>
<td>Immediate success</td>
</tr>
<tr>
<td>Late recurrence</td>
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Values are mean±SD or n (%). NS indicates not significant.
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