Electrical Connections Between Pulmonary Veins
Implication for Ostial Ablation of Pulmonary Veins in Patients With Paroxysmal Atrial Fibrillation

Atsushi Takahashi, MD; Yoshito Iesaka, MD; Yoshihide Takahashi, MD; Ryoko Takahashi, MD; Kenzaburo Kobayashi, MD; Katsumasa Takagi, MD; Osamu Kuboyama, MD; Takeo Nishimori, MD; Hidenobu Takei, MD; Hiroshi Amemiya, MD; Hideomi Fujiwara, MD; Masayasu Hiraoka, MD

Background—Electrical disconnection of the myocardial extensions into arrhythmogenic pulmonary veins (PVs) is recognized as a curative technique for paroxysmal atrial fibrillation (AF). However, the presence of electrical connections between the PVs, which may make achievement of PV disconnection difficult, has not been systematically evaluated.

Methods and Results—Forty-nine consecutive patients with drug-resistant AF underwent ostial radiofrequency (RF) catheter ablation of arrhythmogenic PVs with foci triggering AF. Pacing from inside the targeted PV was performed after each RF delivery to identify the left atrial exit site of the residual venoatrial conduction. Successful PV disconnection was defined as achieving elimination of the PV potentials during sinus rhythm or left atrial pacing, and the loss of left atrial conduction during intra-PV pacing. A total of 112 arrhythmogenic PVs were identified. PV disconnection was achieved with 10±6.1 minutes of RF delivery to the ostia of 101 targeted PVs. In 7 left superior (LS) PVs from 7 patients (14%), the earliest atrial activity was recorded from the left inferior (LI) PV ostium during intra-LSPV pacing after 11±4.7 minutes of RF delivery to the LSPV ostium. Disconnection of these LSPVs was achieved by LIPV disconnection. In the remaining 4 PVs from 4 patients, PV disconnection could not be achieved.

Conclusions—Fourteen percent of the patients had electrical connections between contiguous PVs. In these patients, ostial ablation of an untargeted PV was required for successful targeted PV disconnection. (Circulation. 2002;105:2998-3003.)

Key Words: fibrillation ■ catheter ablation ■ veins ■ atrium

Previous reports demonstrated that atrial fibrillation (AF) could be initiated by focal discharges originating from the myocardial sleeves extending into the pulmonary veins (PVs), and that these foci could be eliminated by restricted radiofrequency (RF) applications. Because of the high recurrence rate and low long-term success rate of focal ablation, the electrical disconnection of the PV and left atrium (LA) at the ostium of arrhythmogenic PVs by means of electrophysiologically or anatomically guided ablation has now been recognized as a better ablative technique to inactivate focal triggers of paroxysmal AF. However, disconnection of the targeted PV may not be achieved if an electrical connection between the PVs exists. The present study was prospectively performed to assess the prevalence and significance of electrical connections between PVs during ostial catheter ablation of the PV in the patients with paroxysmal AF.

Methods

Patient Population
Forty-nine consecutive patients with paroxysmal AF resistant to 3.6±2.1 antiarrhythmic drugs were prospectively studied. They consisted of 46 men and 3 women with a mean age of 51±12 years. All 49 patients had documentation of AF triggered by atrial premature beats on the 12-lead ECG or Holter monitoring before the procedure. Nineteen patients had underlying disease: hypertension in 9 patients, dilated cardiomyopathy in 2, AF tachycardia related to congestive heart failure in 2, ischemic heart disease in 1, and sick sinus syndrome in 5. Transesophageal echocardiograms were performed in all patients 2 days before the procedure. Nineteen patients had underlying disease: hypertension in 9 patients, dilated cardiomyopathy in 2, AF tachycardia related to congestive heart failure in 2, ischemic heart disease in 1, and sick sinus syndrome in 5. Transesophageal echocardiograms were performed in all patients 2 days before the procedure to confirm the absence of intracardiac thrombi. All antiarrhythmic drugs and anticoagulants were discontinued 7 days before hospitalization and on admission, respectively.

Mapping of Ectopic Foci
After informed consent was obtained, all patients underwent an electrophysiological study in the fasting state. Two decapolar and 3 quadripolar catheters were inserted through the right femoral or...
subclavian veins and placed in the lateral right atrium, coronary sinus (CS), superior vena cava, His bundle region, and pulmonary artery to simultaneously map atrial ectopic beats with or without initiating AF. The surface ECG (leads II, III, and VI) filtered through a bandpass of 0.05 to 100 Hz and bipolar intracardiac electrograms filtered from 30 to 500 Hz and amplified at a gain of 0.2 mV/cm were simultaneously recorded with an EP Laboratory system (Bard Electrophysiology). A programmable stimulator (Cardiacstimulator, Nihon Kohden) with a 2-ms pulse width and output of 4 times the diastolic threshold was used. If isolated or repetitive atrial ectopic beats, as well as those initiating AF, were not spontaneously observed, the following provocative maneuvers were performed to elicit atrial premature beats: atrial pacing up to 200 ms, isoproterenol infusion (1 to 2 µg/min), rapid injection of adenosine triphosphate disodium (20 to 60 mg), carotid sinus massage, Valsalva maneuver, or administration of effervescent agents or smoking (because of documented AF initiation during or after meals or smoking in some patients). If these provocative maneuvers were not effective, cardioversion of pacing-induced AF was attempted to convert the AF into sinus rhythm, followed by observation for spontaneous arrhythmia.

When the earliest atrial activity during ectopy was observed in the pulmonary artery or CS, this focus was considered to originate from the LA and a transseptal puncture was performed (except in 8 patients with a patent foramen ovale) for direct LA mapping. Three 6F decapolar steerable catheters (St Jude Medical, Daig Division) were introduced into the LA through a single transseptal puncture site and placed in the right superior (RS), left superior (LS), and left inferior (LI) PVs, and subsequently into the right inferior (RI) PV to confirm the arrhythmogenic PV with the earliest activation from an inferior (LI) PVs, and subsequently into the right inferior (RI) PV to document AF initiation during or after meals or smoking (in some patients). If these provocative maneuvers were not effective, cardioversion of pacing-induced AF was attempted to convert the AF into sinus rhythm, followed by observation for spontaneous arrhythmia.

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Ablation Procedure
A 5000-U intravenous bolus of heparin followed by a continuous infusion of 1000 U/h was administered after the transseptal puncture or before the ablation. For atrial or PV ostial foci, the RF ablation site was chosen on the basis of the earliest bipolar activity. If an intra-PV focus was identified, a circular decapolar catheter (Spiral SC, St Jude Medical, Daig Division) was deployed into the proximal lumen of the PV close to the arrhythmogenic PV ostium (except for the RIPV), as visualized by selective angiography using a 10-mL hand injection of contrast medium through a long sheath (RSPV, LSPV, and LIPV) or NIH catheter (RIPV). RF ablation of arrhythmogenic PVs was performed using the bipoles of the circular catheter or mapping/ablation catheter bipoles (PV-to-LA PV conduction block).

Selective PV angiography was performed after the ablation. All patients received a continuous heparin infusion (1000 U/h) for 5 hours after the procedure and were monitored by telemetry until discharge. Oral anticoagulants were administered for 3 months after ablation.

After discharge, follow-up assessment was through periodic visits to the supervising cardiologist and included monitoring the 24-hour Holter recordings and symptoms monthly for documentation of AF recurrence. In the event of AF recurrence, a repeat ablation was advised.

Statistical Analysis
Continuous data were expressed as mean ± SD. Statistical comparisons were performed with the Student t test, Fisher exact test, or χ² analysis as appropriate. P < 0.05 was considered to be statistically significant.

Results
Localization of Triggering Ectopic Beats
In 49 patients, 112 of 117 ectopic beats with or without triggering AF were identified in the PVs (40 RSPVs, 45 LSPVs, 3 RIPVs, and 24 LIPVs). Forty-one patients had multiple foci. The 5 remaining foci were identified in the atrium or PV ostium in 4 patients with an intra-PV focus. These foci originated from the LA roof in 1 patient, superior vena cava in one, crista terminalis in one, and ostia of the RSPV and LIPV in another.

RF Ablation
In 4 patients with atrial or PV ostial foci, all foci were eliminated with ≥1.2 RF applications at sites 45±16 ms during sinus rhythm or LA pacing (LA-to-PV conduction block), and the loss of LA conduction during intra-PV pacing with an output of 2 to 9.9 V and 2-ms pulse width (which was performed from multiple sites in as circumferential a manner as possible) using the circular catheter or mapping/ablation catheter bipoles (PV-to-LA conduction block).

Figure 1. A, Electrograms recorded circumferentially from LSPV ostium during distal CS pacing. LA-to-LSPV conduction prolonged after 9 minutes of RF delivery to this PV ostium, but PVPs could not be eliminated. B, LSPV-to-LA conduction during intra-PV pacing from bipole 4 to 5 of the circular catheter placed in the LSPV. Note that the earliest atrial activity (arrow) was recorded from the LIPV ostium. LAA indicates LA appendage, and ABLp and ABLd, proximal and distal electrode pair of the ablation catheter, LIPVos, LIPV ostium, LSPV110 through LSPV12, bipolar electrograms from the circular catheter placed in the LSPV ostium; CSp and CSpd, proximal and distal electrode pair of the GS catheter; and St, stimulation.
preceding the ectopic P wave. Elimination of PVPs was achieved with 10±6.1 minutes of RF delivery to the targeted PV ostium in 101 of 112 arrhythmogenic PVs in 49 patients. The earliest atrial activity during intra-targeted PV pacing was always recorded at the ostia of the targeted PVs during ostial ablation procedures for these 101 PVs. In 7 LSPVs from 7 patients (14%), the earliest atrial activity was identified from the LIPV ostium during intra-LSPV pacing after 11±4.7 minutes of RF delivery to the LSPV ostium, which could not eliminate the PVPs (Figures 1 and 2). Elimination of these LSPV potentials was associated with that of the LIPV potentials after 4.2±2.2 minutes of RF delivery to the LIPV ostium, mainly to the superior and/or inferior walls, and fewer RF applications were required at the superior than the inferior wall of the LIPV (Figures 3 and 4). In the remaining 4 PVs (2 LSPVs, 1 LIPV, and 1 RIPV) in 4 patients, elimination of the PVPs could not be achieved because of an intolerable burning sensation in 2 patients (LSPV and LIPV) and the occurrence of a hemopericardium probably due to catheter manipulation when repositioning the catheter into the LA appendage during LSPV ostial ablation in one who required percutaneous drainage.

The inability of LA capture was documented with PVP capture during intra-PV pacing with a mean output of 5.2±1.3 V in 103 of 115 PVs with elimination of the PVPs during sinus rhythm or LA pacing. In one patient with an electrical connection between PVs, unidirectional LSPV-to-LA conduction was observed during intra-LSPV pacing after elimination of LSPV potentials by RF delivery to the LIPV ostium. This conduction was eliminated after LIPV disconnection (Figures 5 and 6). In 3 of 7 patients with electrical connections between PVs, simultaneous recording from circular catheters placed in both PVs demonstrated a synchronized pattern of stable automatic activity dissociated from the LA activity (Figure 7). Moreover, synchronized capture of both PVPs without LA conduction was observed during pacing from inside the LSPV or LIPV in these 7 patients (Figure 8). In the remaining 11 PVs, PVP capture was not clearly visible, but LA capture (which was observed before eliminating the PVPs) was not observed even during
intra-PV pacing with an output of 9.9 V. No far-field capture of the adjacent PV (except for conduction through electrical connections between PVs) was observed in these 115 PVs. Thus, electrical disconnection was achieved in 115 (97%) of 119 targeted PVs and that of all targeted PVs was achieved in 45 patients (92%) in the first ablation session. The procedure and fluoroscopic time were 189/1100640 and 100/1100620 minutes, respectively. Selective angiography performed just after the ablation in all 49 patients revealed no narrowing of the PVs.

There was no significant difference in the age (53/1100615 years versus 51/1100611 years), incidence of LA enlargement (0 patients [0%] versus 7 patients [17%]), structural heart disease (1 patient [14%] versus 4 patients [10%]), or presence of a common ostium in the left PVs (2 patients [29%] versus 3 patients [7%]) between the patients with and without electrical connections between the LSPV and LIPV, respectively.

Repeat Ablation and Follow-Up
Twenty patients (41%) including 4 with unsuccessfully ablated PVs and 1 with an electrical connection between PVs had AF recurrence, and reablation was performed in 13 patients (including 1 with an unsuccessfully ablated PV) 2.9/110061.8 months after the first ablation session. The recovery of ostial PV conduction was documented in 19 of 25 previously disconnected PVs. The ectopic beat originated from 15 previously targeted PVs in 6 patients, including 1 with a new LIPV ostial focus, 1 with 2 untargeted PVs, and 5 with both (5 previously targeted PVs and 10 untargeted PVs). All PVs were successfully disconnected with a 6.3/110064.2-minute RF delivery, and the LIPV ostial focus was ablated by 2 RF applications. However, 4 patients had AF recurrence and 1 underwent a third ablation session with successful disconnection of a previously targeted RSPV.

Of 26 PVs from 13 patients with repeat ablation sessions due to AF recurrence, the angiography revealed a narrowing of the ostium (<25%) in 5 PVs (19%: 3 LSPVs, 2 RSPVs, and 1 LIPV) from 4 patients.

During a follow-up period of 7/110064.1 months, no AF recurrence was documented in the 39 patients (80%) without antiarrhythmic drugs.

Discussion
The present study showed that 14% of patients undergoing ostial ablation of PVs for paroxysmal AF had electrical connections between the LSPV and LIPV identified by confirmation of an LA exit of the residual venoatrial conduction during intra-LSPV pacing and were followed by successful LIPV disconnection. This finding indicates that ostial ablation of contiguous untargeted PV is required for successful targeted PV disconnection in patients with electrical connections between PVs.

Electrophysiological Evidence of Electrical Connections Between PVs
In the present study, the electrical connections between PVs were prospectively assessed by pacing from inside the PV just distal to the ostial ablation site after each RF application. This pacing method allowed the identification of the LA exit for the residual venoatrial conduction during intra-LSPV pacing and were followed by successful LIPV disconnection. This finding indicates that ostial ablation of contiguous untargeted PV is required for successful targeted PV disconnection in patients with electrical connections between PVs.
of AF was observed in 2 PVs and a focal RF application in only one PV was sufficient to restore sinus rhythm. They speculated an insulated connection between the 2 PVs, but evidence of this could not be obtained. Recently, Tritto et al9 reported one case in which spontaneous LSPV automatic discharges, which were dissociated from the LA activation observed after the electrical disconnection of this vein, directly transmitted to the LIPV. In the present study, the same phenomenon was demonstrated after electrical disconnection of both the LSPV and LIPV in 3 of 7 patients with electrical connections between PVs. Moreover, synchronized capture of both the LSPV and LIPV potentials without LA activation was observed during pacing from the intra-LSPV or LIPV in all 7 patients. A recent anatomic examination of the PVs demonstrated that the area of the atrial myocardium between the orifices of the veins draining the same lung varied from 7.3 mm to <3 mm in this series of adult hearts and that 8 of all 20 hearts were <3 mm wide. This finding may imply a potential for myocardial continuity between adjacent PVs, especially in cases with narrow myocardial isthmuses between PVs, and may explain the basis of the conduction between contiguous PVs. Ho et al2 also demonstrated that the myocardial sleeves were thickest in the inferior wall of the LSPV and the superior wall of the LIPV. In the present study, fewer RF applications were required at the superior than the inferior wall of the LIPV ostium in patients with electrical connections between PVs (Figure 4). The reason for this finding may be the influence of previous RF applications to the inferior sector of the LSPV ostium.

Implications for Ostial PV Ablation

On the basis of the knowledge of the AF initiation mechanism by focal discharges in the PVs, electrical disconnection at the PV ostium is now recognized as a better ablative technique to inactivate focal triggers of AF. However, electrical disconnection may not be achieved by ostial ablation to only the targeted PV in patients with electrical connections between the PVs. In this situation, disconnection of the contiguous nontargeted PV is required to achieve successful targeted PV disconnection. The inability to disconnect the PV was demonstrated in 3% to 24% of targeted PVs and may be associated with the presence of electrical connections between PVs in some of these patients. More-
over, recognition of electrical connections between PVs during ostial ablation of PVs prevents unnecessary or excessive RF applications that probably produce postablation PV stenosis.5,6,10

The end point of PV disconnection has usually been defined as the elimination of PVPs during sinus rhythm or LA pacing.5–7 However, this criterion neglects conduction block from the PV to LA at the PV ostium. In the present study, we further included the inability of LA capture during intra-PV pacing in addition to the above criterion, which resulted in all but 1 PV demonstrating no LA conduction after achievement of the LA-to-PV conduction block. In one LSPV with an electrical connection to the LIPV, LA conduction was observed during intra-PV pacing after elimination of LSPV potentials, indicating unidirectional block. These findings suggest that the assessment of the PV-to-LA conduction by intra-PV pacing is important for confirming complete PV disconnection as well as detection of an electrical connection between PVs.

Study Limitations
The present study did not provide information about the precise anatomic location of electrical connections between the PVs, because mapping during intra-targeted PV pacing was performed only at the venoatrial junction of the targeted and untargeted PVs to identify the PV responsible for the venoatrial conduction. Also, LIPV ostial mapping with the use of a circular catheter during intra-LSPV pacing before ablation (which was not performed in our study) may be helpful in identifying the precise location of an electrical connection between PVs. RF ablation was performed at the ostium of the arrhythmogenic PV as proximal as possible in the present study, but ablation performed at different sites such as more distal sites in the PVs may not result in a similar prevalence of electrical connections between PVs. PV disconnection at the common ostium may demonstrate the same findings as in our 7 patients with electrical connections between PVs after ablation, but the LSPV and LIPV were separately targeted in our series of patients. The presence of a residual venoatrial breakthrough point at the targeted PV that cannot be detected as a result of insufficient mapping of the targeted PV ostium after several RF applications may lead to a misdiagnosis of electrical connections between the PVs. However, in this case, targeted PV disconnection would never be achieved by ostial ablation of the untargeted PV.

Conclusions
Extensive ostial PV mapping during intra-targeted PV pacing allowed for the identification of residual conduction between contiguous PVs that made targeted PV disconnection impossible. Recognition of these electrical connections between the PVs is important for the practical application of the ablation procedure to achieve PV disconnection in patients with paroxysmal AF, because ostial ablation of untargeted PVs is required for successful targeted PV disconnection and to minimize unnecessary RF applications.

References
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