Cause of Very Late Recurrence of Atrial Fibrillation or Flutter After Catheter Ablation for Atrial Fibrillation

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The major mechanism underlying the early recurrence of atrial fibrillation (AF) after ablation is mainly reconnection of the isolated pulmonary vein (PV); however, the mechanism responsible for very late recurrence (VLR) has not been fully elucidated. The purpose of the present study was to investigate the mechanism underlying VLR. The study population included 150 consecutive patients with AF who underwent a second session of catheter ablation because of recurrence. We divided them into 2 groups according to the point of initial AF recurrence: the late recurrence group (LR group, initial recurrence 3 to 12 months after ablation, n = 124) and the VLR group (initial recurrence >12 months after ablation, n = 26). We identified PVs with ectopic foci (trigger PVs) in the first procedure and checked their electrical reconnection in the second procedure. The prevalence of PV reconnection and trigger PV reconnection were significantly lower in the VLR group than in LR group (LR vs VLR, 90% vs 69% and 48% vs 27%, p = 0.007 and p = 0.045, respectively). In the VLR group, left ventricular systolic and diastolic function were significantly worse than in the LR group, and more patients in the VLR group required non-PV trigger ablation in the second session than did those in the LR group (30% vs 54%, p = 0.034). In conclusion, electrical PV reconnection contributed less to VLR than to LR. Progression of the AF substrate might be an important mechanism responsible for VLR. **(Am J Cardiol 2013;111:552−556)**

The pulmonary veins (PVs) are the crucial source of the triggers that initiate atrial fibrillation (AF),[1−4] and electrical PV isolation is an effective therapeutic option for AF.[5−8] Previous reports have shown that patients who undergo catheter ablation for AF experience an initial recurrence >1 year after the procedure.[9−11] Several studies have revealed that the major mechanism of AF recurrence is electrical reconnection of isolated PVs[12−16]; however, the mechanism responsible for very late recurrence (VLR), defined as the first AF recurrence >1 year after AF ablation, with a 3-month blanking period, has not been fully elucidated. To investigate the mechanisms responsible for VLR, we compared the baseline patient characteristics and electrophysiologic findings at the second session of catheter ablation between patients with and without VLR.

Methods

The present study is a retrospective, single-center, observational study. A 3-month blanking period after ablation was included. Recurrence type was categorized according to the time of initial AF recurrence: late recurrence (LR) and VLR. LR and VLR was defined as recurrence within 3 to 12 months after catheter ablation for AF and >1 year after catheter ablation for AF, respectively.

The data from 150 consecutive patients with AF (mean age 59 ± 10 years, 128 men) who underwent a second session of catheter ablation from September 2005 to October 2011 at our institution were analyzed. Of these, 124 patients had experienced LR (LR group) and 26 had experienced VLR (VLR group). All patients provided written informed consent for AF ablation. The preoperative evaluations included transthoracic echocardiography, transesophageal echocardiography, and multidetector computed tomography for all patients. Antiarrhythmic drugs (AADs) were discontinued >3 half-lives before the procedure. The exclusion criteria were as follows: severe valvular heart disease, an enlarged left atrium (diameter >50 mm), age >80 years, longstanding persistent AF for >10 years, and hypertrophic cardiomyopathy.

An electrophysiologic study and radiofrequency catheter ablation were performed as follows. A 6F decapolar catheter was placed in the coronary sinus by way of the median antebrachial vein, and a 7F decapolar catheter was placed in the superior vena cava and right atrium by way of the femoral vein. Three long sheaths were introduced into the left atrium using a single trans-septal puncture technique. After catheter placement, a standard electrophysiologic study was performed. Electrical cardioversion was performed in cases with persistent AF. The PVs were categorized into 3 types: (1) a normal PV, a PV without premature

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See page 555 for disclosure information.

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Table 1
Baseline patient characteristics

Variable	LR (n = 124)	VLR (n = 26)	p Value
Age (yrs)	60 ± 9	56 ± 13	0.064
Men	106 (85%)	22 (85%)	>0.99
Height (cm)	166.7 ± 8.2	169.7 ± 8.0	0.09
Weight (kg)	68 [60−77]	67 [59−72]	0.58
Body mass index (kg/m^2)	24.5 [22.3−26.6]	23.3 [21.5−24.4]	0.07
Obesity (body mass index >25 kg/m^2)	51 (41%)	6 (23%)	0.085
Paroxysmal/nonparoxysmal atrial fibrillation	64/60	13/13	0.82
Duration of atrial fibrillation (mo)	60 [20−120]	39 [15−96]	0.31
$CHADS_2$ score*	1 [0−1.5]	1 [0−1]	0.11
Hypertension	66 (53%)	11 (42%)	0.31
Diabetes mellitus	24 (19%)	2 (8%)	0.25
Left atrial diameter (mm)	38 [35−43]	38 [31−41]	0.20
Left atrial end diastolic volume (ml)	74 [59−96]	64 [49−85]	0.11
Left atrial ejection fraction (%)	21 [16−37]	22 [16−36]	0.79
Left ventricular ejection fraction (%)	63 ± 10	57 ± 10	0.009
Mitral annulus velocity (cm/s)	11.2 ± 7.5	8.1 ± 3.1	0.038
Creatinine (mg/dl)	0.8 [0.7−1.0]	0.9 [0.8−1.0]	0.34
Brain natriuretic peptide (pg/ml)	85 [36−159]	69 [29−97]	0.18
C-reactive protein (mg/dl)	0.055 [0.03−0.13]	0.035 [0.02−0.09]	0.14

Data are expressed as mean ± SD, n (%), or median [interquartile range].
* Congestive heart failure, hypertension (blood pressure consistently >140/90 mm Hg or hypertension treated with medication), age ≥75 yrs, diabetes mellitus, previous stroke or transient ischemic attack.

atrial complexes with a coupling interval of <350 ms, (2) a trigger PV, a PV with reproducible premature atrial complexes with a coupling interval of <350 ms that did not initiate AF during observation, and (3) an AF trigger PV, a PV with premature atrial complexes initiating recurrence of AF. The prevalence of trigger and AF trigger PVs was examined with and without isoproterenol infusion. PV isolation was guided by fluoroscopy or a 3-dimensional mapping system. We used a nonirrigated ablation catheter with an 8-mm tip (Fantasista, Japan Lifeline, Tokyo, Japan) before December 2009, and an irrigated ablation catheter with a 3.5-mm tip (Navistar Thermocool, Biosense Webstar, Diamond Bar, California) after January 2010 for mapping and ablation. All patients underwent extensive PV isolation using a "double lasso" technique. For 15 to 30 seconds at each point, radiofrequency energy was delivered ≤30 W, with a temperature limit of 45°C using an irrigated catheter or ≤35 W with a temperature limit of 50°C using a nonirrigated catheter. A nonirrigated catheter was used for 93% of the first procedures, because irrigated catheters were not available in the early phase of the present study in Japan. During the first procedure, circumferential PV isolation was performed successfully in all patients. If atrial flutter or atrial tachycardia coexisted or was induced by atrial burst pacing, the isthmus was ablated. If it was still difficult to maintain sinus rhythm, additional linear ablation of the left atrium roof and bottom of the left atrium, mitral valve isthmus, ablation of the complex fractionated atrial electrogram, isolation of the superior vena cava, and ablation of the cavotricuspid isthmus were performed. We tried to ablate non-PV premature atrial complexes if they triggered AF or appeared frequently and constantly. The strategy for the second procedure was similar to that for the first.

All patients were hospitalized for 3 days after the ablation procedure with continuous rhythm monitoring. A prescription of AADs at discharge was decided by the patient' attending physician, if necessary. Although the AADs were supposed to be discontinued for patients without recurrence during the 3 months after the procedure, the prescription of AADs in the outpatient clinic was finally decided by the attending physicians. All patients were scheduled for visits to the outpatient clinic at 1, 2, 3, 6, 9, and 12 months after ablation and every 6 months thereafter. An electrocardiogram was performed at every visit. Holter electrocardiography, transthoracic echocardiography, and multidetector computed tomography were performed 3 months after ablation. Recurrence was defined as recurrent symptoms and/or documented AF on the electrocardiogram after a 3-month blanking period after ablation. Clinical success was defined as a ≥75% reduction in the number of AF episodes, duration of AF episodes, or

Table 2
Prevalence of trigger pulmonary veins (PVs) and reconnection of isolated pulmonary veins (PVs)

Variable	LR (n = 124)	VLR (n = 26)	p Value
First catheter ablation			
Trigger pulmonary vein	102 (82%)	20 (77%)	0.72
Atrial fibrillation trigger pulmonary vein	63 (51%)	9 (35%)	0.20
Nonpulmonary vein foci	80 (65%)	18 (69%)	0.65
Second catheter ablation			
Total pulmonary vein reconnection	111 (90%)	18 (69%)	0.0067
Reconnected trigger pulmonary vein	60 (48%)	7 (27%)	0.045
Reconnected atrial fibrillation trigger pulmonary vein	42 (34%)	4 (15%)	0.10
Nonpulmonary vein foci	94 (76%)	19 (73%)	0.76