

# Incidence and Predictors of Pulmonary Vein Stenosis Following Catheter Ablation of Atrial Fibrillation Using the Anatomic Pulmonary Vein Ablation Approach: Results from Paired Magnetic Resonance Imaging

JUN DONG, M.D.,\* CHANDRASEKHAR R. VASAMREDDY, M.D.,\* VINOD JAYAM, M.D.,\*  
 DARSHAN DALAL, M.D.,\* TIMM DICKFELD, M.D., PH.D.,\* ZAYD ELDDADAH, M.D.,\*  
 GLENN MEININGER, M.D.,\* HENRY R. HALPERIN, M.D., M.A.,\*,†,¶  
 RONALD BERGER, M.D., PH.D.,\* DAVID A. BLUEMKE, M.D., PH.D.,¶  
 and HUGH CALKINS, M.D.\*

From the \*Department of Medicine, †Department of Biomedical Engineering, and ¶Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

**Pulmonary Vein Stenosis After Atrial Fibrillation Ablation.** *Introduction:* There are currently no studies systematically evaluating pulmonary vein (PV) stenosis following catheter ablation of atrial fibrillation (AF) using the anatomic PV ablation approach.

*Methods and Results:* Forty-one patients with AF underwent anatomic PV ablation under the guidance of a three-dimensional electroanatomic mapping system. Gadolinium-enhanced magnetic resonance (MR) imaging was performed in all patients prior to and 8–10 weeks after ablation procedures for screening of PV stenosis. A PV stenosis was defined as a detectable ( $\geq 3$  mm) narrowing in PV diameter. The severity of stenosis was categorized as mild ( $< 50\%$  stenosis), moderate (50–70%), or severe ( $> 70\%$ ). A total 157 PVs were analyzed. A detectable PV narrowing was observed in 60 of 157 PVs (38%). The severity of stenosis was mild in 54 PVs (34%), moderate in five PVs (3.2%), and severe in one PV (0.6%). All mild PV stenoses displayed a concentric pattern. Moderate or severe PV stenosis was only observed in patients with an individual encircling lesion set. Multivariable analysis identified individual encircling lesion set and larger PV size as the independent predictors of detectable PV narrowing. All patients with PV stenosis were asymptomatic and none required treatment.

*Conclusions:* The results of this study demonstrate that detectable PV narrowing occurs in 38% of PVs following anatomic PV ablation. Moderate or severe PV stenosis occurs in 3.8% of PVs. The high incidence of mild stenosis likely reflects reverse remodeling rather than pathological PV stenosis. The probability of moderate or severe PV stenosis appears to be related to creation of individual encircling rather than encircling in pairs lesion. (*J Cardiovasc Electrophysiol*, Vol. 16, pp. 845-852, August 2005)

*atrial fibrillation, ablation, pulmonary vein*

## Introduction

Pulmonary vein (PV) stenosis is an important complication of catheter ablation of atrial fibrillation (AF). It has been reported in up to 21% of patients with AF undergoing segmental PV isolation.<sup>1-6</sup> This procedure involves the delivery of radiofrequency (RF) current either within the PVs or to the ostial portion of the PVs, with the goal of achieving electrical isolation of all PVs as determined with the use of circumferential multipolar mapping catheters. More recently, Pappone and colleagues<sup>7-10</sup> developed an alternative approach to catheter ablation of AF, referred to as anatomic PV ablation. This procedure involves the delivery of multiple RF application in a circumferential fashion around the two right and two left PV ostia, as well as the creation of several linear lesions

guided by electroanatomic mapping. Despite the widespread adoption of the anatomic PV ablation approach, no prior study has systematically evaluated the severity and incidence of PV stenosis following this procedure. Therefore, it was the aim of this study to determine the incidence, severity, and predictors of PV stenosis following anatomic PV ablation by the means of paired magnetic resonance (MR) imaging.

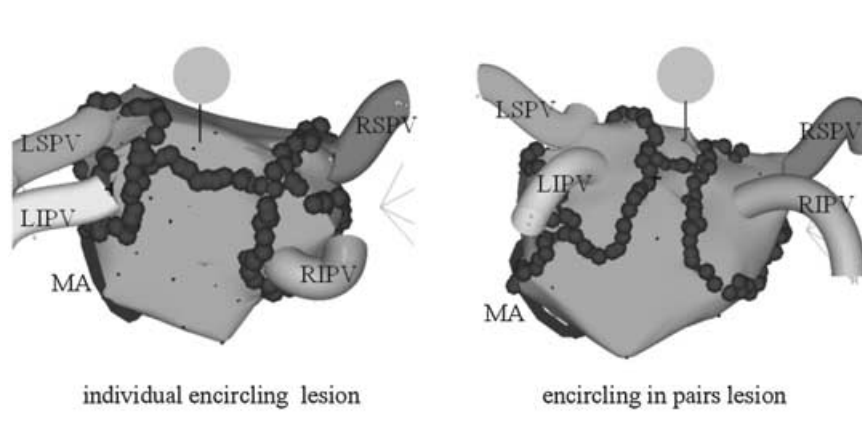
## Methods

### Study Patients

The patient population included 41 consecutive patients (18 females,  $56 \pm 10$  years) who underwent anatomic PV ablation as an initial ablation strategy for treatment of symptomatic drug refractory AF. MR imaging was obtained prior to and 8–10 weeks after catheter ablation. Structural heart disease was present in eight patients (20%). Four patients had coronary artery disease, one had hypertensive heart disease, one had nonischemic cardiomyopathy, one had surgical corrected atrial septal defect, and one had mitral valve prolapse. Twelve patients had paroxysmal AF, 12 had persistent AF, and 17 had permanent AF. LA size averaged  $45 \pm 8.5$  mm.

Address for correspondence: Hugh Calkins, M.D., Johns Hopkins Hospital, Carnegie 592, 600 N Wolfe Street Baltimore, MD, 21287-0409. Fax: 410-614-1345; E-mail: hcalkins@jhmi.edu

Manuscript received 25 September 2004; Revised manuscript received 20 January 2005; Accepted for publication 25 January 2005.



**Figure 1.** Two types of lesion sets. Anatomic maps of the left atrium and pulmonary veins, posteroanterior view, show individual encircling lesion (left panel) and encircling in pairs lesion (right panel). See text for a further description. Dark brown points indicate the ablation sites. LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; MA = mitral annulus.

Informed written consent was obtained in all patients under a protocol approved by the Johns Hopkins Institutional Review Board.

#### **Electrophysiologic Study and Catheter Ablation**

After gaining access through the right and left femoral veins, two quadripolar catheters were introduced into the right atrium. One 6- or 7F catheter was placed at His-bundle position and another 7F deflectable electrode catheter with 2–5–2 mm interelectrode spacing was inserted into the coronary sinus. A single transseptal puncture was then performed under fluoroscopic guidance and one long vascular sheath (SR0, St. Jude Medical, Minnetonka, MN, USA) was introduced into the left atrium (LA). Following the transseptal puncture an initial intravenous bolus of 5000 IU heparin was given, and repeated doses of heparin were given to maintain the activated clotting time >300 seconds. The long sheath was flushed with heparinized saline at a flow rate of 3 mL/minute during the entire procedure. A quadripolar deflectable 8-mm tip catheter (Navistar, Biosense Webster, Diamond Bar, CA, USA) was inserted into the LA via the long sheath for mapping and ablation.

The LA anatomy was reconstructed by point-to-point sequential sampling of the endocardial sites using a three-dimensional electroanatomic mapping system (CARTO, Biosense Webster). The LA appendage and the mitral annulus were demarcated. Mapping of each PV was performed by placing the Navistar catheter 2–4 cm inside each PV and slowly pulling it back to the LA under fluoroscopic guidance. During this course, virtual tubes were created by CARTO to represent the main body of the PVs. The ostium of each PV was identified based on the results of selective biplane PV angiography and fluoroscopic visualization of the catheter tip entering cardiac silhouette with simultaneous decrease in impedance and appearance of atrial potential.<sup>8,9,11,12</sup>

Circumferential lesions encircling right and left PVs ostia were created by delivering RF current to the tip of the Navistar catheter under the guidance of CARTO. Linear ablation lesions were also created at the cavotricuspid isthmus, the mitral isthmus, and on the posterior wall of the LA. In 24 patients additional linear lesions were created between the superior and inferior PVs resulting in an individual encir-

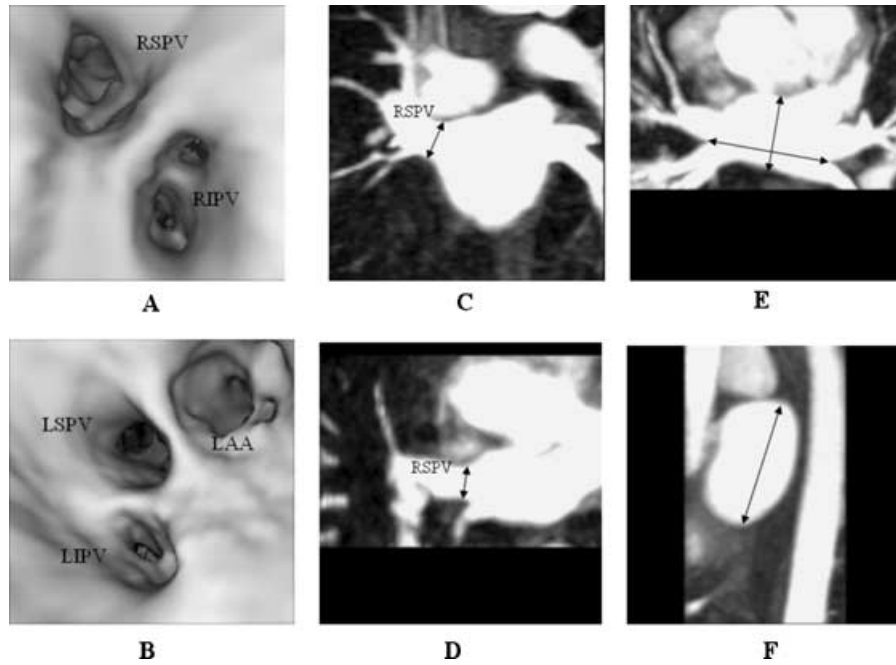
cling lesion in comparison to a encircling in pairs lesion in the remaining 17 patients (Fig. 1). The RF energy was applied continuously with repositioning of the catheter tip every 10–20 seconds at a target temperature of 55°C and a maximum power of 70 W in a temperature control mode. The target was to reduce local bipolar voltage by 80% or to <0.1 mV at the ablation sites.<sup>9</sup> The intention was to place RF lesions at least 1–2 cm away from the PV ostia to avoid PV stenosis. However, in some cases RF lesions were deployed at the anterior portion of the left superior PV ostium due to its proximity to the LA appendage.<sup>13</sup> Continuous impedance monitoring was used to avoid inadvertent RF current delivery within the PVs.<sup>8,12</sup> RF energy was immediately discontinued when a  $\geq 10 \Omega$  increase in impedance was observed. As an anatomy based ablation strategy, no assessments such as differential pacing were performed to demonstrate conduction block at the ablation lines created in the LA.

Patients were discharged home the following day. They were instructed to take low molecular weight heparin (Lovenox) until their protime reached therapeutic level. Each patient was seen in follow-up 8 weeks following the ablation procedure. Thereafter patients who live locally were followed at 2–3 months intervals. Many of our patients do not live in this region of the country and we therefore allowed follow-up through their local cardiologist and/or internist. For patients not being followed at our center, we obtained follow-up information by contacting both patient and their following physician. Each of these patients was being seen on a regular basis by their referring physician. Patients who reported symptoms compatible with an arrhythmia underwent event monitoring. All patients were followed for a minimum of 3 months following the catheter ablation procedure. A successful outcome was defined as the absence of any symptomatic atrial arrhythmias beyond the first month without the use of antiarrhythmic drugs. No efforts such as periodic 7-day Holter monitoring were made to screen asymptomatic occurrence of atrial arrhythmias.

#### **Magnetic Resonance Imaging**

##### *Image acquisition*

Within 1 week prior to and 8–10 weeks after ablation procedures, all patients underwent Gadolinium-enhanced MR



**Figure 2.** Measurement of pulmonary vein (PV) and left atrium (LA) diameters. A: Virtual endoscopic image of the right PVs. B: Virtual endoscopic image of the left PVs. C: Oblique coronal image with targeted maximum intensity projection parallel to long axis of the right superior PV (RSPV). Superoinferior diameter was measured at the junction between the RSPV and LA (arrow). The junction was defined as point of inflection between the PV wall and LA wall. D: Oblique axial image and measurement of anteroposterior diameter of the RSPV by using the same method mentioned above. E: Oblique axial view of the LA. Transverse diameter of the LA was defined as the distance between the midpoint of the right and left PVs. Anteroposterior diameter was measured at the midpoint of transverse diameter (arrows). F: Sagittal image of the LA. Longitudinal diameter was also measured at the midpoint of transverse diameter (arrow). LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RIPV = right inferior pulmonary vein; LAA = left atrium appendage.

imaging with a 1.5-T MR imaging system (Signa Horizon LX; GE Medical Systems) using the protocol we reported in detail previously.<sup>13</sup> Briefly, MR angiograms (MRAs) were obtained with a breath-hold three-dimensional fast spoiled gradient-echo imaging sequence in the coronal plane. The acquisition time was approximately 15 seconds. Maximum intensity projection (MIP) and multiplanar reformations were performed to reconstruct images of the PV and LA. Virtual endoscopic images (VEIs) were reconstructed to determine PV anatomy and ostium location (Fig. 2A,B).

#### Measurement of PV diameters

Initial evaluation of the MR imaging scans was performed with 20- to 40-mm-thick MIPs and VEIs. The superoinferior (SI) and anteroposterior (AP) diameters of each PV were then assessed in 8- to 10-mm-thick slices of two long-axis MIP PV images (oblique coronal and oblique axial images). The slice thickness was selected because it usually covered more than half of the maximal PV diameter. To determine the long axis of the PV, axial and coronal tomograms at the junction of the PV and LA were displayed, and then oblique coronal and oblique axial images were identified parallel to each PV. The PV ostium was defined as the point of inflection between the LA wall and the PV wall (Fig. 2C,D). The ostium of right superior PV (RSPV) was difficult to detect because of its funnel shape. To overcome this obstacle, multiple oblique coronal planes were used for detecting the upper wall of the right inferior PV (RIPV) as a marker of the border between the LA and PV.<sup>13</sup> The diameter of each PV was assessed at the ostium and 5, 10, and 15 mm more distal.

#### Measurement of LA size and calculation of LA volume

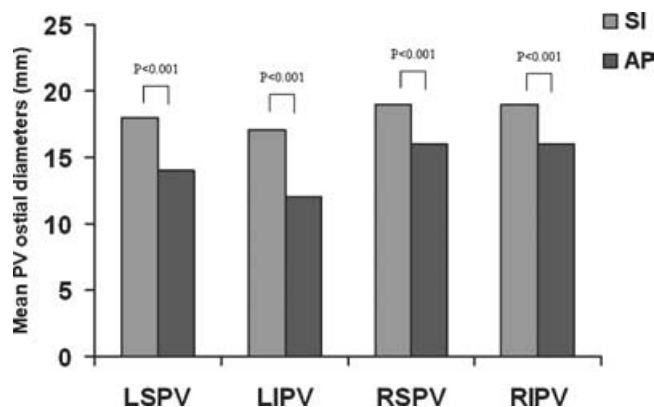
The size of the LA was measured according to the technique of Ho et al.<sup>14</sup> The measurement of transverse diameter of the LA was defined as the distance between the midpoint of the right and left PVs in oblique axial images. The AP and longitudinal diameters were measured at the midpoint of the transverse diameter in oblique axial and sagittal images, respectively (Fig. 2E,F). The LA volume was calculated using the following equation considering that LA resembles an ovoid cylinder:

$$\text{LA volume} = \pi \times \text{transverse diameter} \times \text{AP diameter} \\ \times \text{longitudinal diameter} / 4.$$

All diameters were measured with the use of a digital caliper on the three-dimensional original digital data set to the nearest millimeter by two investigators (J.D. and V.Y.) who were blinded to the lesion sets and clinical outcomes. The intraobserver variability and interobserver variability of the MR imaging measurements of PV size were  $0.9 \pm 1.2$  mm and  $1.1 \pm 1.4$  mm, respectively.

#### Assessment of PV stenosis

A PV stenosis was defined as narrowing of the PV (main vessel or first branch) diameter  $\geq 3$  mm, as the nominal resolution of the source images was 2.4 mm.<sup>13</sup> The percentage diameter reduction and patterns of PV stenosis (concentric or eccentric) were recorded. The severity of stenosis was categorized as mild ( $<50\%$  stenosis), moderate (50–70%), or severe ( $>70\%$ ).<sup>13</sup> Both the oblique coronal view and oblique axis view were used for measuring PV narrowing.



**Figure 3.** Comparison between superoinferior (SI) and anteroposterior (AP) pulmonary vein (PV) ostial diameters. LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein.

### Statistical analysis

The data are presented as mean  $\pm$  SD, counts or percentages, as appropriate. Comparison was performed by Student's *t*-test for continuous variables and chi-square test or Fisher's exact test for categorical variables. Longitudinal logistic and linear regression analyses were used to determine predictors of PV stenosis and percentage reduction of PV diameter, respectively. Longitudinal linear regression was performed to detect the correlation between PV diameter reduction and LA volume reduction. All tests were two-tailed;  $P < 0.05$  was considered significant. All statistical analyses were performed by using STATA statistical software package (version 8.0, College Station, TX, USA).

## Results

### Clinical Outcomes of Catheter Ablation

A successful outcome was achieved in 25 patients (61%) after a mean follow-up of  $5.7 \pm 2.7$  months. No patients experienced symptoms consistent with PV stenosis. Two patients developed atypical atrial flutter during first month follow-

up. The atrial flutter resolved spontaneously in one patient and was successfully cardioverted in the other patient. At the last follow-up visit, the former had AF relapse and the latter remained in sinus rhythm on antiarrhythmic drug.

### PV Anatomic Patterns

The PV anatomy was visualized in each study patient. There were 157 PVs in the 41 patients. Twenty-six patients (63%) had a typical pattern of four PVs. A left common PV and a right middle PV (RMPV) were observed in 12 patients (29%) and 5 patients (12%), respectively. Two patients had a right common PV ( $n = 1$ ) or a right top PV ( $n = 1$ ).<sup>15</sup> PV ostia were oval in shape with the SI diameter greater than the AP diameter (Fig. 3).

### Incidence and Characteristics of PV Stenosis Following Anatomic PV Ablation

A PV stenosis, as defined as a detectable ( $\geq 3$  mm) reduction in PV diameter, was observed in 60 of 157 PVs (38%). It is notable that in 19 of these 60 stenosed PVs (32%), the diagnosis of PV stenosis was solely based on narrowing of the AP diameter. Table 1 summarizes the location and severity of PV stenosis observed in this study. The degree of stenosis was mild in 54 PVs (34%), moderate in 5 PVs (3.2%), and severe in 1 PV (0.6%).

Shown in Figure 4 are representative examples of the different patterns of PV stenosis observed in this study. Figure 4A,B show examples of a concentric mild PV stenosis. It is notable that all mild PV stenoses were concentric. Among six PVs with moderate or severe stenosis, four (2 RIPVs, 1 RSPV, 1 RMPV) manifested as an eccentric stenosis. The remaining two moderate or severe stenoses were concentric (two left inferior PVs). Focal narrowing in PVs with eccentric stenosis was centrally located (i.e., at the inferior wall for superior PV and at the superior wall for inferior PV). Figure 4C,D show examples of moderate PV stenosis, a RSPV with focal narrowing at its inferior wall. Figure 4E,F show the only severely stenosed PV (left inferior PV) observed in this study, with a 72% ostial narrowing in conjunction with occlusion of the superior branch of the left inferior PV.

When analyzed based on patients rather than PVs, 30 of 41 patients (73%) had  $\geq 1$  stenosed PV (range: 1–4). Twenty-four patients (59%) had only mild PV stenosis, five (12%) had moderate PV stenosis, and one (2.4%) had severe PV stenosis. Of note, none of the patients with PV stenosis required therapy.

### Predictors of PV Stenosis

In order to determine predictive factors of PV stenosis, the potential predictors of PV stenosis listed in Table 2 were included in a longitudinal logistic regression model. In the univariable analysis, preablation PV diameter (larger) was identified the predictor of PV stenosis and individual encircling lesion had a borderline *P* value of 0.06. Multivariable analysis revealed that both individual encircling lesion and preablation PV diameter were the independent predictors of PV stenosis following ablation procedure (Table 2). Creation of an individual encircling lesion was associated with a 2.7-fold higher risk of PV stenosis than a encircling in pairs lesion. In comparison to PVs with smaller diameter, PVs with larger diameter were more likely to suffer from PV stenosis.

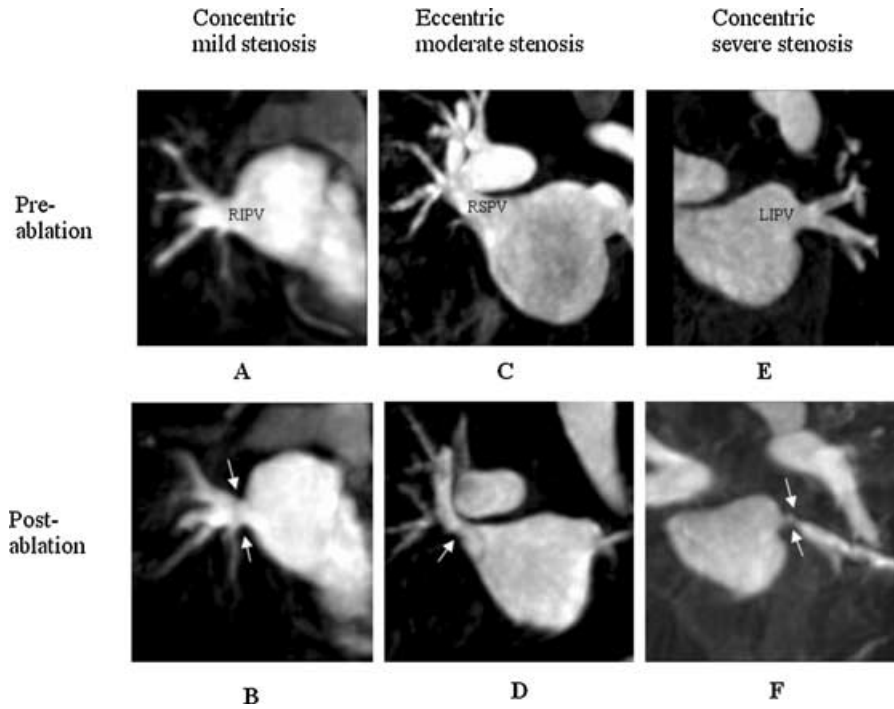
**TABLE 1**

Location and Severity of Pulmonary Vein Stenosis

	Mild Stenosis (<50%)	Moderate Stenosis (50–70%)	Severe Stenosis (>70%)	Total
LSPV (n = 29)	5 (17)	0	0	5 (17)
LIPV (n = 29)	8 (28)	1 (3.4)	1 (3.4)	10 (35)
RSPV (n = 40)	18 (45)	1 (2.5)	0	19 (48)
RIPV (n = 40)	15 (38)	2 (5)	0	17 (43)
LCPV (n = 12)	8 (67)	0	0	8 (67)
RMPV (n = 5)	0	1 (20)	0	1 (20)
RCPV (n = 1)	0	0	0	0
RTPV (n = 1)	0	0	0	0
Total (n = 157)	54 (34)	5 (3.2)	1 (0.6)	60 (38)

Values are given as n (%).

LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LCPV = left common pulmonary vein; RMPV = right middle pulmonary vein; RCPV = right common pulmonary vein; RTPV = right top pulmonary vein.



**Figure 4.** Pulmonary vein stenosis following anatomic pulmonary vein ablation. Top, baseline magnetic resonance images. Bottom, follow-up magnetic resonance images. See text for a further description. LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein.

In a longitudinal linear regression model, both creation of an individual encircling lesion (coefficient 2.1,  $P = 0.001$ ) and preablation PV diameter (larger) (coefficient 0.85,  $P < 0.001$ ) were found to be the predictors of percentage reduction of PV diameter after adjusting for other potential predictors listed in Table 2.

A relationship was also observed between the lesion set and the incidence of moderate or severe PV stenosis. Moderate or severe PV stenosis was observed in 6 of 94 PVs (6.4%) in patients who underwent ablation using the individual encircling lesion as compared with none of the 63 PVs (0%) in patients who underwent ablation using a encircling in pairs lesion ( $P = 0.08$ ). Similarly, the incidence of moderate or severe PV stenosis was greater among patients having individual encircling lesion than among those having encircling in pairs lesion (6/24 [25%] vs 0/17 [0%],  $P = 0.03$ ) (Fig. 5). Due to very low incidence of moderate or severe PV stenosis, no multivariable analysis could be performed to determine the predictors for moderate or severe PV stenosis.

**LA Volume Reduction**

The longitudinal, AP and transversal diameters were  $62 \pm 8$  mm,  $36 \pm 7.5$  mm, and  $57 \pm 7.4$  mm before catheter ablation, respectively. After ablation procedures, these diameters decreased to  $58 \pm 7.8$  mm,  $35 \pm 8.5$  mm, and  $54 \pm 8.6$  mm, respectively. Accordingly, the LA volume reduced from  $103 \pm 36$  mL to  $89 \pm 42$  mL. Subgroup analysis revealed that significant LA volume reduction only occurred in patients who had a successful outcome (Fig. 6).

**Correlation Between PV Diameter and LA Volume Reduction**

Following anatomic PV ablation, the PV ostial diameter in SI dimension and LA volume decreased by  $6.4 \pm 13\%$  and  $15 \pm 16\%$ , respectively. Longitudinal linear regression analysis detected a correlation in percentage reduction between PV ostial diameter and LA volume ( $P = 0.05$ ).

**TABLE 2**  
Predictors of Pulmonary Vein (PV) Stenosis Following Anatomic PV Ablation

	Unadjusted Odds Ratio (95% CI)	P Value	Adjusted Odds Ratio (95% CI)	P Value
Age	1.02 (0.98–1.06)	0.43	1.00 (0.95–1.06)	0.90
Female	1.62 (0.71–3.71)	0.25	2.23 (0.71–7.00)	0.17
Individual encircling lesion	2.28 (0.98–5.33)	0.06	2.71 (1.08–6.83)	0.03
Preablation PV diameter	1.08 (1.01–1.16)	0.04	1.11 (1.02–1.20)	0.02
Structural heart disease	1.10 (0.50–2.40)	0.82	0.74 (0.31–1.77)	0.50
Paroxysmal AF	0.74 (0.32–1.72)	0.49	0.82 (0.25–2.76)	0.75

AF = atrial fibrillation; CI = confidence interval.

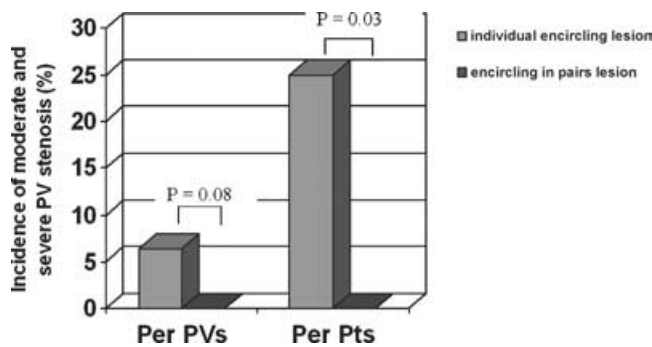


Figure 5. Impact of lesion sets on moderate and severe pulmonary vein (PV) stenosis.

### Discussion

To the best of our knowledge, this study is the first to systematically evaluate the incidence of PV stenosis using either CT or MR imaging following catheter ablation of AF using the anatomic PV approach. There are two main findings in this study. First, this study demonstrated that a detectable reduction in PV diameter is present in 38% of PVs following anatomic PV ablation. Moderate and severe PV stenosis is observed in 3.2% and 0.6% of PVs, respectively. No patient developed main vessel occlusion and no patient had symptomatic PV stenosis requiring treatment. And second, the use of an individual encircling lesion set that requires RF ablation between the ipsilateral PVs, and PV size were identified as independent predictors of detectable PV narrowing. All moderate and severe PV stenoses were associated with an individual encircling lesion set.

Over the past decade, PV stenosis has emerged as a unique and highly significant complication of catheter ablation of AF.<sup>5,16-19</sup> Not only is PV stenosis difficult to diagnose and often misdiagnosed for other conditions such as lung cancer or pulmonary embolism, but PV stenosis may also be life threatening and is difficult to treat.<sup>16,18,20</sup> In an attempt to reduce the incidence of PV stenosis and improve the efficacy of AF ablation, the ablation target of electrophysiologists performing this procedure has moved from within the PVs to the extraostial portion of the PVs or PV antrum.<sup>2,7-9,21-25</sup> This has been facilitated both by the use of three-dimensional electroanatomic mapping systems and by the use of in-

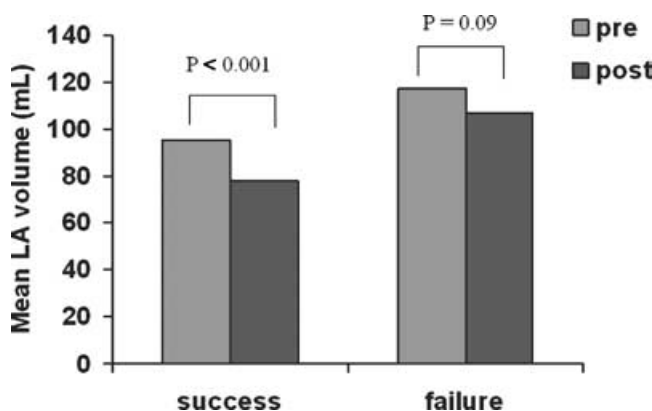


Figure 6. Left atrium (LA) volume reduction following anatomic pulmonary vein ablation.

tracardiac ultrasound.<sup>7-9,23-25</sup> One of the most commonly performed approaches today is anatomic PV ablation, developed by Pappone et al.<sup>7-10</sup> This procedure involves the use of a three-dimensional electroanatomic mapping system (CARTO). The lesion set described by Pappone et al. involves the creation of an individual encircling lesion around the two left and two right PVs as well as the creation of additional linear lesions. Oral et al.<sup>23</sup> modified this technique slightly and abandoned the lesion between the ipsilateral PVs, resulting in two encircling in pairs lesions.

Despite a major shift in the approaches used for catheter ablation of AF and the importance of PV stenosis, there have been no systemic evaluations of incidence and severity of PV stenosis following catheter ablation of AF using the anatomic PV ablation approach with MR or CT imaging. Although Pappone et al.<sup>10</sup> reported that none of 589 patients who underwent this procedure developed PV stenosis, the evaluation of PV stenosis was limited to transesophageal echocardiograms. With the use of paired MR imaging, in the current study we found that a detectable ( $\geq 3$  mm) narrowing in PV diameter is common following anatomic PV ablation, occurring in 38% of PVs. Moderate (50–70%) and severe ( $>70\%$ ) PV stenosis is observed in 3.2% and 0.6% of PVs, respectively. In this series, no patient developed main vessel occlusion and no patient developed symptomatic PV stenosis requiring treatment. Independent predictors of detectable PV narrowing were the individual encircling lesion set and the PV size (larger).

The high incidence of PV stenosis, as defined as a detectable ( $\geq 3$  mm) reduction in PV diameter, and the presence of any patients with moderate or severe PV stenosis were surprising and unanticipated, as every effort was made to deliver RF energy outside the PV ostia. There are several potential explanations for these findings. First, although PV angiography, electroanatomic mapping, and impedance monitoring were utilized in an attempt to avoid delivery of RF energy to the PV ostia or within the PVs, these techniques are imperfect. Electroanatomic mapping, for example, relies on the patient's position remaining unchanged throughout the procedure. With patient movement, the three-dimensional electroanatomic reconstruction of the LA and PVs may not accurately reflect true anatomy. Similarly, PV angiography is typically performed immediately prior to the start of PV ablation. Not only does this provide only a crude two-dimensional representation of true PV anatomy, but patient movement later in the procedure may also result in misalignment of the true PV anatomy with that reflected by the PV angiograms. Although impedance monitoring provides on line feedback to the location of the ablation catheter relative to the PV, a recent study found no significant difference in impedance between PV ostial and LA sites.<sup>12</sup> Therefore, it is possible for movement of the ablation catheter into the PV ostia to be missed. Second, the RF lesions might be placed indeed at the same location—PV ostia, as in the PV isolation approach because the incidence of significant PV stenosis ( $>50\%$ ) after anatomic PV ablation observed in the current study is similar to that after segmental PV isolation.<sup>3</sup> The high incidence of mild PV stenosis (defined as a reduction in diameter of  $<50\%$ ), likely reflects PV reverse remodeling rather than pathological PV stenosis. This hypothesis is based on the observation that all of the mild PV stenoses were concentric rather than eccentric. In contrast, four of six

moderate or severe PV stenoses were eccentric. This explanation is also supported by the finding that the degree of reduction in PV size correlated with the degree of LA volume reduction. Moreover, the results of multivariate analysis of detectable PV narrowing suggest that individual encircling lesion set produces more pronounced effect on PV reverse remodeling and larger PVs are more prone to PV reverse remodeling. Based on these results, we would propose that the term "PV stenosis" be defined in the future as a detectable eccentric PV narrowing and/or a reduction in PV diameter of >50%.

We believe LA volume reduction following ablation observed in the present study is due to the effect of sinus rhythm enhanced reverse remodeling rather than atrial fibrosis caused by ablation because significant atrial volume reduction was only found in patients with a successful outcome.

A limitation of our study was that the follow-up MR imaging was performed only 8–12 weeks following catheter ablation. It has been well established that PV stenosis may progress over time.<sup>3–6</sup> Therefore we cannot be certain that the patients in our study with evidence of PV stenosis may progress over time and ultimately develop symptomatic PV stenosis requiring treatment. It will, therefore, be important that follow-up studies are performed to address this important topic.

There are several clinical implications to the results of this study. First, it is clear that moderate or severe PV stenosis may occur following catheter ablation using the anatomic PV ablation approach. This finding should compel physicians performing this procedure to continue to obtain routine post procedure MR or CT imaging, or at least to have a heightened awareness of symptoms suggestive of PV stenosis. Second, the fact that moderate or severe PV stenosis was only observed following anatomic PV ablation using an individual encircling lesion set suggests that an encircling in pairs lesion may be more appropriate. It is notable that Oral et al.<sup>23</sup> reported excellent efficacy of catheter ablation of AF using the modified anatomic PV approach with this type of encircling in pairs lesion. And finally, the results of this study suggest that the term "PV stenosis" should be reserved for patients who develop eccentric and/or significant (>50%) PV narrowing.

## References

- Haissaguerre M, Jais P, Shah DC, Garrigue S, Takahashi A, Lavergne T, Hocini M, Peng JT, Roudaut R, Clementy J: Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. *Circulation* 2000;101:1409-1417.
- Haissaguerre M, Shah DC, Jais P, Hocini M, Yamane T, Deisenhofer I, Chauvin M, Garrigue S, Clementy J: Electrophysiological breakthroughs from the left atrium to the pulmonary veins. *Circulation* 2000;102:2463-2465.
- Dill T, Neumann T, Ekinci O, Breidenbach C, John A, Erdogan A, Bachmann G, Hamm CW, Pitschner HF: Pulmonary vein diameter reduction after radiofrequency catheter ablation for paroxysmal atrial fibrillation evaluated by contrast-enhanced three-dimensional magnetic resonance imaging. *Circulation* 2003;107:845-850.
- Arentz T, Jander N, Von Rosenthal J, Blum T, Furmaier R, Gornandt L, Josef Neumann F, Kalusche D: Incidence of pulmonary vein stenosis 2 years after radiofrequency catheter ablation of refractory atrial fibrillation. *Eur Heart J* 2003;24:963-969.
- Saad EB, Rossillo A, Saad CP, Martin DO, Bhargava M, Erciyes D, Bash D, Williams-Andrews M, Beheiry S, Marrouche NF, Adams J, Pisano E, Fanelli R, Potenza D, Raviele A, Bonso A, Themistoclakis S, Brachmann J, Saliba WI, Schweikert RA, Natale A: Pulmonary vein stenosis after radiofrequency ablation of atrial fibrillation: Functional characterization, evolution, and influence of the ablation strategy. *Circulation* 2003;108:3102-3107.
- Purerfellner H, Cihal R, Aichinger J, Martinek M, Nesser HJ: Pulmonary vein stenosis by ostial irrigated-tip ablation: Incidence, time course, and prediction. *J Cardiovasc Electrophysiol* 2003;14:158-164.
- Pappone C, Oreto G, Lamberti F, Vicedomini G, Loricchio ML, Shpun S, Rillo M, Calabro MP, Conversano A, Ben Haim SA, Cappato R, Chierchia S: Catheter ablation of paroxysmal atrial fibrillation using a 3D mapping system. *Circulation* 1999;100:1203-1208.
- Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G, Salvati A, Dicandia C, Mazzone P, Santinelli V, Gulletta S, Chierchia S: Circumferential radiofrequency ablation of pulmonary vein ostia: A new anatomic approach for curing atrial fibrillation. *Circulation* 2000;102:2619-2628.
- Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F, Salvati A, Dicandia C, Calabro MP, Mazzone P, Ficarra E, Di Gioia C, Gulletta S, Nardi S, Santinelli V, Benussi S, Alfieri O: Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: Efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. *Circulation* 2001;104:2539-2544.
- Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P, Gulletta S, Gugliotta F, Pappone A, Santinelli V, Tortoriello V, Sala S, Zangrillo A, Crescenzi G, Benussi S, Alfieri O: Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: Outcomes from a controlled nonrandomized long-term study. *J Am Coll Cardiol* 2003;42:185-197.
- Vasamreddy CR, Jayam V, Lickfett L, Nasir K, Bradley DJ, Eldadah Z, Dickfeld T, Donahue K, Halperin HS, Berger R, Calkins H: Technique and results of pulmonary vein angiography in patients undergoing catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15:21-26.
- Cheung P, Hall B, Chugh A, Good E, Lemola K, Han J, Tamirisa K, Pelosi F Jr, Morady F, Oral H: Detection of inadvertent catheter movement into a pulmonary vein during radiofrequency catheter ablation by real-time impedance monitoring. *J Cardiovasc Electrophysiol* 2004;15:674-678.
- Kato R, Lickfett L, Meininger G, Dickfeld T, Wu R, Juang G, Angkeow P, LaCorte J, Bluemke D, Berger R, Halperin HR, Calkins H: Pulmonary vein anatomy in patients undergoing catheter ablation of atrial fibrillation: Lessons learned by use of magnetic resonance imaging. *Circulation* 2003;107:2004-2010.
- Ho SY, Sanchez-Quintana D, Cabrera JA, Anderson RH: Anatomy of the left atrium: Implications for radiofrequency ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 1999;10:1525-1533.
- Lickfett L, Kato R, Tandri H, Jayam V, Vasamreddy CR, Dickfeld T, Lewalter T, Luderitz B, Berger R, Halperin H, Calkins H: Characterization of a new pulmonary vein variant using magnetic resonance angiography: Incidence, imaging, and interventional implications of the "right top pulmonary vein." *J Cardiovasc Electrophysiol* 2004;15:538-543.
- Robbins IM, Colvin EV, Doyle TP, Kemp WE, Loyd JE, McMahon WS, Kay GN: Pulmonary vein stenosis after catheter ablation of atrial fibrillation. *Circulation* 1998;98:1769-1775.
- Scanavacca MI, Kajita LJ, Vieira M, Sosa EA: Pulmonary vein stenosis complicating catheter ablation of focal atrial fibrillation. *J Cardiovasc Electrophysiol* 2000;11:677-681.
- Ernst S, Ouyang F, Goya M, Lober F, Schneider C, Hoffmann-Riem M, Schwarz S, Hornig K, Muller KM, Antz M, Kaukel E, Kugler C, Kuck KH: Total pulmonary vein occlusion as a consequence of catheter ablation for atrial fibrillation mimicking primary lung disease. *J Cardiovasc Electrophysiol* 2003;14:366-370.
- Saad EB, Marrouche NF, Saad CP, Ha E, Bash D, White RD, Rhodes J, Prieto L, Martin DO, Saliba WI, Schweikert RA, Natale A: Pulmonary vein stenosis after catheter ablation of atrial fibrillation: Emergence of a new clinical syndrome. *Ann Intern Med* 2003;138:634-638.
- Qureshi AM, Prieto LR, Latson LA, Lane GK, Mesia CI, Radvansky P, White RD, Marrouche NF, Saad EB, Bash DL, Natale A, Rhodes JF: Transcatheter angioplasty for acquired pulmonary vein stenosis after radiofrequency ablation. *Circulation* 2003;108:1336-1342.
- Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, le Metayer P, Clementy J:

- Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659-666.
22. Haissaguerre M, Sanders P, Hocini M, Hocini M, Hsu LF, Shah DC, Scavee C, Takahashi Y, Rotter M, Pasquie JL, Garrigue S, Clementy J, Jais P: Changes in atrial fibrillation cycle length and inducibility during catheter ablation and their relation to outcome. *Circulation* 2004;109:3007-3013.
  23. Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, Veerareddy S, Pelosi F Jr, Morady F: Catheter ablation for paroxysmal atrial fibrillation: Segmental pulmonary vein ostial ablation versus left atrial ablation. *Circulation* 2003;108:2355-2360.
  24. Marrouche NF, Martin DO, Wazni O, Gillinov AM, Klein A, Bhargava M, Saad E, Bash D, Yamada H, Jaber W, Schweikert R, Tehou P, Abdul-Karim A, Saliba W, Natale A: Phased-array intracardiac echocardiography monitoring during pulmonary vein isolation in patients with atrial fibrillation: Impact on outcome and complications. *Circulation* 2003;107:2710-2716.
  25. Marchlinski FE, Callans D, Dixit S, Gerstenfeld EP, Rho R, Ren JF, Zado E: Efficacy and safety of targeted focal ablation versus PV isolation assisted by magnetic electroanatomic mapping. *J Cardiovasc Electrophysiol* 2003;14:358-365.