Pulmonary Vein Stenosis After Radiofrequency Ablation of Atrial Fibrillation
Functional Characterization, Evolution, and Influence of the Ablation Strategy

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Background—Pulmonary vein (PV) stenosis is a complication of ablation for atrial fibrillation. The impact of different ablation strategies on the incidence of PV stenosis and its functional characterization has not been described.

Methods and Results—PV isolation was performed in 608 patients. An electroanatomic approach was used in 71 and circular mapping in 537 (distal isolation, 25; ostial isolation based on PV angiography, 102; guided by intracardiac echocardiography, 140; with energy delivery based on visualization of microbubbles, 270). Severe (≥70%) narrowing was detected in 21 patients (3.4%), and moderate (50% to 69%) and mild (<50%) narrowing occurred in 27 (4.4%) and 47 (7.7%), respectively. Severe stenosis occurred in 15.5%, 20%, 2.9%, 1.4%, and 0%, respectively. Development of symptoms was correlated with involvement of >1 PV with severe narrowing (P=0.01), whereas all patients with mild and moderate narrowing were asymptomatic. In the latter group, lung perfusion (V/Q) scans were normal in all but 4 patients. All patients with severe stenosis had abnormal perfusion scans.

Conclusions—V/Q scans are useful to assess the functional significance of PV stenosis. Mild and moderate degrees of PV narrowing are not associated with development of symptoms and seem to have no or minimal detrimental effect on pulmonary flow. The incidence of severe PV stenosis seems to be declining with better imaging techniques to ensure ostial isolation and to guide power titration. Mild narrowing 3 months after ablation does not preclude future development of severe stenosis and should be assessed with repeat imaging studies. (Circulation. 2003;108:3102-3107.)

Key Words: fibrillation ■ veins ■ ablation ■ stenosis

Pulmonary vein (PV) stenosis is a well-known complication of PV isolation for the treatment of atrial fibrillation (AF). Although frequently asymptomatic, it can be associated with severe respiratory symptoms that cause significant morbidity. Predictive factors for the development of PV stenosis could be application of lesions inside the veins and inappropriate energy delivery.

Isolation of all PVs has become the primary goal of catheter ablation of AF. In recent years, a variety of strategies have been developed to achieve isolation. The impact of each treatment approach on the incidence of PV stenosis has not been reported. This study reports on the occurrence of PV stenosis according to the use of different ablation techniques. We have also characterized the functional impact of different degrees of PV narrowing and their evolution over time.

Methods

Patients
From January 1998 to December 2002, 608 patients (mean age, 51.3 years; 81.1% male) underwent PV isolation for treatment of drug-refractory, symptomatic AF. Demographic characteristics are presented in Table 1. Informed consent was obtained from all patients. Data from these procedures were entered into an established elec-
Summary of study methods. Pts. indicates patients.

Figure 1. Summary of study methods. Pts. indicates patients.

TABLE 1. Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>No PV Narrowing (n=513)</th>
<th>All PV Narrowing (n=95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean±SD)</td>
<td>54.0±11.0</td>
<td>50.6±13.4</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>418 (81.5)</td>
<td>75 (78.9)</td>
</tr>
<tr>
<td>AF duration, y (mean±SD)</td>
<td>5.4±3.6</td>
<td>4.5±2.1</td>
</tr>
<tr>
<td>Left atrial size, cm (mean±SD)</td>
<td>4.2±0.6</td>
<td>4.3±0.6</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>52.8±8.3</td>
<td>54.3±5.6</td>
</tr>
<tr>
<td>Structural heart disease, n (%)</td>
<td>133 (26.0)</td>
<td>23 (24.2)</td>
</tr>
<tr>
<td>Antiarrhythmic drugs, n (range)</td>
<td>3 (1–7)</td>
<td>3 (1–5)</td>
</tr>
<tr>
<td>Paroxysmal AF, n (%)</td>
<td>268 (52.2)</td>
<td>50 (52.4)</td>
</tr>
<tr>
<td>Persistent AF, n (%)</td>
<td>70 (13.7)</td>
<td>27 (28.6)</td>
</tr>
<tr>
<td>AF, n (%)</td>
<td>175 (34.1)</td>
<td>18 (19.0)</td>
</tr>
</tbody>
</table>

trophysiology laboratory database approved by the Cleveland Clinic Foundation Institutional Review Board.

Procedure Description

Transesophageal echocardiography was performed in all patients to exclude the presence of left atrial thrombus before the procedure. Instrumentation of the right and left atrium was performed as described previously.

Isolation of the PVs was performed by use of different strategies (Figure 1), as follows. (1) For electroanatomic mapping, the PVs were delineated by use of the Carto system (Biosense-Webster), and radiofrequency lesions were delivered around their circumference by a 4-mm-tip catheter (Navistar, Biosense-Webster). (2) For distal isolation guided by circular mapping, a decapolar circular catheter (Lasso, Biosense Webster) was placed in a stable position inside the PVs (>5 mm from the ostium), and isolation was attempted by targeting recorded PV potentials. (3) For ostial isolation guided by PV angiography, selective PV angiography was performed to determine the ostium of the veins during adenosine-induced asystole. The circular catheter was then placed at the defined ostium, where isolation was performed. (4) For ostial isolation guided by intracardiac echocardiography (ICE), the circular mapping catheter was placed at the PV–left atrial junction as determined by ICE. (5) For ostial isolation guided by ICE associated with power titration directed by formation of microbubbles, the delivery of radiofrequency energy was controlled by progressively increasing the power (watts) until microbubbles were visualized. This was considered an early manifestation of tissue overheating, and when it was present, energy was immediately titrated downward until microbubbles subsided. Energy delivery was discontinued in case microbubble generation did not settle.

In groups 1–4, radiofrequency energy was delivered in the temperature-controlled mode, with a maximum temperature of 50°C and a maximum power of 50 W. In group 5, the same parameters were used for the cooled-tip catheters, and maximum power was 70 to 100 W if an 8-mm-tip catheter was used.

Follow-Up

An arrhythmia transmitter was given to all patients before hospital discharge for detection of recurrent AF and was repeated at 3 months after the procedure or at any time symptoms recurred.

Routine follow-up visits were made at 3, 6, and 12 months after the procedure. In the first 176 patients undergoing isolation with circular mapping and in additional 73 patients in the ICE+microbubbles monitoring group, a spiral computed tomogram (CT) of the PVs was obtained before and at 1, 3, 6, and 12 months after the procedure, as we have described previously. The scan was obtained irrespective of the development of symptoms as a screening method to detect PV stenosis. In the remaining patients, the first CT scan was routinely performed =3 months after the procedure (Figure 1). If any PV narrowing was detected at 3 months, CT was repeated at 6 and 12 months to evaluate lesion progression. CT was also performed as a diagnostic test whenever symptoms compatible with PV stenosis developed. PV stenosis was defined as mild, moderate, or severe if <50%, between 50% and 69%, and ≥70% luminal narrowing was evident, respectively. Patients with severe stenosis were referred for PV angiography and angioplasty.

Quantitative pulmonary V/Q scans were performed in 17 patients (36.2%) and 25 patients (92.6%) with mild or moderate PV narrowing, respectively, and in all patients with severe stenosis (see Table 3). In the latter group, V/Q scans were obtained before and serially after the interventional procedure.

Statistical Analysis

Continuous variables are expressed as mean±SD and were compared by the unpaired t test. Categorical variables were compared by χ² analyses or Fisher’s exact test. Results with P<0.05 were considered statistically significant.

Results

Overall, 95 of 608 patients (15.6%) developed PV narrowing (severe, 21 patients, 3.4%; moderate, 27 patients, 4.4%; mild, 47 patients, 7.7%) diagnosed 3.5±2.2 months after the ablation procedure (Table 1). A median of 4 (range, 2 to 4) PVs were ablated per patient, and the median number of stenosed PVs was 2 (range, 1 to 3) per patient. The left PVs were exclusively involved in 18 of 21 patients with severe stenosis. Table 2 summarizes the clinical presentation and the distribution of stenosis among the PVs. Complications related to the procedure were infrequent and included cerebrovascular accidents in 4 patients (0.7%), tamponade in 3 (0.5%), and hematomas in 3 (0.5%).

Different Ablation Strategies

A total of 71 patients underwent ablation guided by electroanatomic mapping, of which 11 (15.5%) developed severe PV stenosis. The circular mapping technique was used in 537 patients, and 10 (1.8%) developed severe PV stenosis. In the latter group, stenosis developed in 5 of 25 patients (20%) ablated distally in the PV and in 3 of 102 (2.9%) of those who received ostial ablation guided by selective PV angiography.

ICE was used in 410 patients. In 140 patients, ICE was used to guide ostial positioning of the circular catheter. In this group,
1.4% of the patients (2 of 140) developed severe PV stenosis. In the subsequent 270 patients, ICE was also used to guide energy delivery according to the visualization of microbubbles. No patients developed severe PV stenosis with the use of this technique. Figure 2 summarizes the incidence of severe PV stenosis according to the ablation strategy used. The overall homogeneity test indicated that the probability of PV stenosis was associated with the ablation strategy (P<0.001).

At the 3-month spiral CT, mild PV narrowing was present in 47 patients (7.7%), and moderate stenosis was seen in 27 patients (4.4%), all of whom were asymptomatic. Lung perfusion (V/Q) scans were performed in 42 (76.2%) of these patients and showed normal perfusion to the corresponding lung in 38 (90.5%). All 4 patients with V/Q mismatch had exclusive involvement of a single right PV (right inferior in 3 patients and right superior in 1) and showed a very small area with perfusion mismatch. Table 3 summarizes the V/Q scan findings according to the severity of PV stenosis. No patients developed symptoms, perfusion abnormalities, or evidence of pulmonary hypertension after 6 to 16 months of follow-up.

### Evolution of PV Narrowing

In 249 patients, spiral CT scans were obtained before and 1, 3, 6, and 12 months after the ablation procedure. Overall, increasing PV narrowing to a different class, including the patients starting with a normal scan, was demonstrated in 22 patients (8.8%), whereas regression of PV narrowing to a different class was observed in 26 (10.4%). Of the 95 patients with PV narrowing, follow-up CT scan showed no change in class of narrowing in 47. Progression and regression of PV narrowing without change of class was seen in 5 of 47 (10%) and 14 of 47 (30%), respectively. The remaining patients showed stable PV anatomy over time.

Evolution of PV narrowing between the 1-month and 3-month CTs was evident in 8 of 102 patients (7.8%) of the angiography-guided group, in 5 of 74 (6.7%) of the ICE group, and in 3 of 73 (4.1%) of the ICE + microbubbles group. Progression of narrowing after the third month was less frequent and occurred in 3 of 102 patients (2.9%), 2 of 74 (2.7%), and 1 of 73 (1.4%) in these groups, respectively. Progression from mild or moderate narrowing to severe stenosis was observed in 3 of 74 patients (4%), 1 of which occurred within 3 months after ablation; 2 patients had progression from moderate to severe stenosis between the 3- and 6-month follow-up CT scans. Figure 3 shows detailed information on the evolution of PV stenosis. No patients with normal spiral CT at 3 months had stenosis at the 6- and 12-month CTs. Instead, 7.6% (15 of 197) of the patients with normal CT 1 month after the ablation showed narrowing at the 3-month scan.

### PV Angiography and Intervention

Diagnostic PV angiography was performed in 19 of 21 patients with severe stenosis. Two patients had 1 PV completely occluded without any narrowing in the other veins. Development of symptoms was related to the involvement of >1 PV (P=0.01, Figure 4). Complete occlusion of ≥1 PV was observed on the CT scans of 11 patients, 3 (27.2%) of which were completely asymptomatic. All the symptomatic patients also had another PV affected with either severe stenosis or concomitant total occlusion. From a total of 15 PVs judged to be completely occluded by the spiral CT scan, 7 were confirmed by angiography, thus precluding any interventional procedure. In 1 patient with severe stenosis of 3 PVS, pulmonary hypertension developed and resolved after dilatation. Balloon angioplasty was performed in 17 patients, and 10 had stents implanted. Significant symptomatic improvement was achieved in 10 patients (59%) (from mean...
NYHA functional class 3.1. 

Discussion

Main Findings

PV stenosis is a complication of PV isolation for the treatment of AF. The use of ICE has been shown to be useful in enhancing visualization of intracardiac structures. 

Our experience reinforces the proposition that real-time imaging could be valuable in preventing severe PV stenosis. In addition, continuous visualization associated with energy titration based on the generation of microbubbles contributed to successful proximal isolation of all PVs.

Progression of PV stenosis beyond the third month after ablation is rare. More commonly, the degree of narrowing remains stable or improves. Also, no change in lung perfusion is seen when the left PVs are involved until the degree of narrowing approaches 70% of the PV lumen. When stenosis occurs in the right PVs, however, small areas of perfusion defects can be seen with degrees of narrowing ranging from 55% to 69%. This difference probably arises because the pressure may be lower in the right PVs, thus facilitating the development of a pressure gradient at lower degrees of narrowing. Many patients with severe narrowing or complete occlusion of a single PV are asymptomatic.

Importance of Ostial Isolation

Definition of the PV–left atrial junction is crucial for successful PV isolation. It seems intuitive that distal isolation leaves behind a significant amount of PV tissue that carries the potential for triggering AF, leading to high recurrence rates. In addition, ostial isolation reduces the risk of developing PV stenosis. Thus, reliable and precise delineation of the PV ostia seems important.

Our initial experience with isolation using electroanatomic mapping to delineate the PVs proved to be disappointing, with isolation observed in only 31% of treated veins and with severe stenosis developing in 15.5% of patients. Stenosis remained high (20%) in the selected group of 25 patients who underwent distal isolation guided by circular mapping. The distal position was used because it provided a more stable location for placement of the circular catheter and for energy application.

Once it became clear that we had to avoid lesions inside the veins, selective PV angiography was used to determine the ostia. This approach decreased the incidence of severe stenosis to ~3%. However, in our series, the use of ICE was associated with the most considerable decrease in the occurrence of stenosis. When used only to guide ostial positioning of the circular catheter, it reduced severe stenosis to 1.4%. It is likely that angiography is not always reliable for adequate
ostial visualization because of the streaming effect of the contrast in the vein and the frequent gradual funneling of the PV junction into the left atrial cavity. That is true even when selective injections and adenosine to reduce the motion effect of the beating heart are used. In this respect, ICE provides continuous visualization of the ostium, allowing online monitoring of catheter position and precise return to the desired location in case of dislodgment.

Importance of Energy Titration
Risk factors for the development of PV stenosis, although yet to be completely defined, include energy delivery inside the veins,3,14,15 vein size, and use of excessive power during radiofrequency application.2,16

Traditional methods for titration of energy delivery, such as tip temperature and impedance measures, may not be accurate.17 This is especially true for left-side procedures, during which the use of excessive power may result in thromboembolic complications. Thus, the development of a reliable method to achieve more accurate energy delivery is needed, and visualization of microbubbles by ICE seems a suitable option. Not only the incidence of PV stenosis but also the recurrence rates are considerably minimized, as we reported recently.18 Indeed, it is remarkable that we have had no patients with severe stenosis since this strategy has been introduced. The rationale for microbubble-guided power titration lies in the premise that adequate tissue heating cannot be predicted simply by monitoring impedance and temperature. Formation of a few scattered microbubbles is believed to reflect the early manifestation of overheating.18,19 When this occurs, energy has to be gradually decreased until their generation subsides. However, if this phenomenon cannot be controlled and progresses, tissue desiccation will result, creating the milieu for coagulum formation and PV stenosis. Therefore, the goal of power titration guided by ICE imaging is to prevent the brisk generation of microbubbles, which usually precedes impedance rise.18

Management of PV Stenosis
A high degree of suspicion is required to promptly diagnose PV stenosis, not only because it can mimic more prevalent respiratory and cardiovascular syndromes but also because diagnostic tests can be misleading, as we and others described previously.7,20,21 This seems to be the case even with V/Q scans, which can be consistent with the diagnosis of pulmonary embolism. However, V/Q scans, when properly interpreted, may be determinant in characterizing the functional relevance of the stenosis. As a matter of fact, severely decreased flow to the affected lung is seen consistently in patients with stenosis approaching 70% of the PV lumen, as opposed to no abnormalities in those with mild narrowing and no or minimal perfusion abnormalities in those with moderate degrees of narrowing.

Of note, complete occlusion or severe narrowing of a single PV never resulted in pulmonary hypertension, and these patients were frequently asymptomatic or had mild symptoms. In our series, we recommend PV dilatation for patients with luminal narrowing of ≥70%, irrespective of the presence of symptoms. The rationale for intervening in these patients lies in the unknown likelihood of developing pulmonary hypertension with long-term follow-up as well as the risk of lesion progression7,16,22 to total occlusion, which could preclude intervention. Whether this aggressive approach is appropriate requires additional studies in larger series. Indeed, in patients either with complete occlusion of a single PV or who refused dilatation because of the lack of symptoms, no adverse outcome was seen at follow-up.

Finally, PV angioplasty was associated with a significant increase in lung flow and improvement of symptoms. However, restenosis rates seem high, and stenting may not provide much improvement, although the numbers are too small to make meaningful conclusions.

Limitations
The present study is a retrospective analysis of consecutive patients referred for AF ablation. The use of different strategies and technologies evolved over time. Thus, the influence of a learning curve23 on the results cannot be definitively excluded. However, that learning curve, although important, is usually surpassed after ~50 to 100 cases and thus would be less influential on the results later in the series. Also, the small number of patients with PV stenosis and the relatively short follow-up may preclude definitive conclusions about the clinical and hemodynamic consequences on the pulmonary circulation.

Conclusions
The incidence of severe PV stenosis after ablation of AF seems to be declining with the use of periprocedural real-time imaging with ICE to ensure ostial isolation and guide power titration during energy delivery. V/Q scans are a useful test to assess the functional significance of PV narrowing. Mild narrowing 3 months after ablation can progress to severe stenosis and should not be ignored. Complete occlusion or severe stenosis of a single PV is seldom associated with development of symptoms or pulmonary hypertension. Whether PV stenosis should always be corrected requires additional studies in larger series.

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References


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