Incidence of pulmonary vein stenosis 2 years after radiofrequency catheter ablation of refractory atrial fibrillation


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Received 16 October 2002; revised 16 December 2002; accepted 18 December 2002

Aims Pulmonary vein ablation offers the potential to cure patients with atrial fibrillation. In this study, we investigated the incidence of pulmonary vein stenosis after radiofrequency catheter ablation of refractory atrial fibrillation by systematic long-term follow-up.

Methods and results Forty-seven patients with refractory and highly symptomatic atrial fibrillation underwent radiofrequency catheter ablation of arrhythmogenic triggers inside the pulmonary veins and/or ostial pulmonary vein isolation with conventional mapping and ablation technology. These patients had follow-up examinations at 2 years with transoesophageal doppler-echo and/or angiographic resonance imaging for the evaluation of the pulmonary veins. Seventy-seven percent of the patients were free from atrial fibrillation, 51% were without antiarrhythmic drugs, and 26% were on previously ineffective antiarrhythmic drug therapy. However, 13 of the 47 patients showed significant pulmonary vein stenosis or occlusion. Only three of these 13 patients complained of dyspnoea. Distal ablations inside the pulmonary vein were associated with a 5.6-fold higher risk of stenosis than ostial ablations.

Conclusions At 2-year follow-up, the risk of significant pulmonary vein stenosis/occlusion after radiofrequency catheter ablation of refractory atrial fibrillation with conventional mapping and ablation technology was 28%. Distal ablations inside smaller pulmonary veins should be avoided because of the higher risk of stenosis than ablation at the ostium.

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KEYWORDS
Atrial fibrillation; Ablation; Pulmonary vein stenosis

Introduction

Atrial fibrillation may be due to discharging focal activity, primarily located in the pulmonary veins. Radiofrequency catheter ablation of such arrhythmia triggers is feasible and can eliminate atrial fibrillation. Pulmonary vein stenosis has been reported as a complication of this procedure. However, systematic long-term follow-up data regarding the success rate and the incidence of pulmonary vein stenosis are not yet available. The purpose of the study was to investigate the incidence of pulmonary vein stenosis 2 years after the ablation procedure.
Methods

Patients (N=47) had pulmonary vein ablation for highly symptomatic paroxysmal (more than two episodes per week) or persistent (more than 4 weeks) atrial fibrillation. Atrial fibrillation was resistant to more than three antiarrhythmic drugs, including class I and III drugs. All patients were scheduled to undergo assessment of pulmonary vein patency by transoesophageal doppler-echo and angio magnetic resonance imaging 2 years after the initial procedure. In addition, a 24 h holter monitoring was performed. In all patients with pulmonary vein stenosis magnetic resonance imaging and transoesophageal doppler-echo were repeated 3–6 months after the 2-year follow-up.

Electrophysiologic study and ablation procedure

Transseptal puncture was performed for mapping of the left atrium and pulmonary veins if no patent foramen ovale was found. Ten patients were treated with focal radiofrequency ablation inside the pulmonary vein at sites of early impulse formation to eliminate the trigger. In 25 patients, an ostial isolation ablation procedure of the arrhythmogenic pulmonary veins was performed using two standard ablation catheters as described by Haissaguerre et al. in 12 patients, both methods were combined (focal trigger ablation and ostial isolation). The pulmonary vein ostium was determined by angiography and local electrogram characteristics (amplitude and timing of pulmonary vein potentials versus atrial potentials). The pulmonary vein isolation was performed as ostial as the stability of the catheter allowed. The ablation site was identified by circumferential mapping of the pulmonary vein ostium. The ablation was performed at the site with the earliest pulmonary vein electrogram during sinus rhythm or coronary sinus pacing. Catheter stability during ablation was checked by fluoroscopy; ablation was stopped immediately if the ablation catheter apparently moved inside the vein or dropped out of the vein. The endpoint of ablation was the elimination of all pulmonary vein activity distal to the ablation site.

Maximum ablation temperature and power were 55 °C and 30–35 W, respectively (radiofrequency generator Osypka, HAT 300, Grenzach-Wylen, Germany).

A selective pulmonary vein angiography was performed before and after ablation. During repeated procedures for atrial fibrillation recurrences the ablation was only performed after confirmation of pulmonary vein patency by angiography.

Anticoagulation (INR>2.5) was stopped 3 months after the procedure if stable sinus rhythm was present, but was reintroduced if pulmonary vein stenosis was detected during follow-up.

Twenty-four hour holter monitoring

Atrial fibrillation was defined as irregular atrial activity lasting for more than 30 s.

Magnetic resonance imaging

Patients were positioned on the table of a 1.5 T imager (Magnetom Sonata, Siemens, Erlangen, Germany) and imaging was performed with a body array coil as a receiver. Gadodiamid (18–22 ml; Nycomed, Braunschweig, Germany) was injected intravenously at a flow rate of 3 ml/s. The acquisition of the images was ECG-gated within a breath hold. Imaging parameters used for the series were as follows: repetition time second/echo time second/Flash 3-D, 1.72/0.6/20°; matrix, 256×126; field of view, 400×320 mm; and section thickness, 2 mm. Partitions of 36 images were acquired performing nine measurements repeatedly. Post-processing included maximum intensity projection (MIP). Subtraction of the arterial phase was performed.

Pulmonary vein anatomy was assessed on the angio magnetic resonance imaging raw image and after 3-D reconstruction. The pulmonary vein ostium was determined at the greatest angle change of tangents drawn millimetre for millimetre through the pulmonary vein wall at the junction zone of the pulmonary vein to the left atrium. A decrease in pulmonary vein diameter by ≥50% was considered significant.

Transoesophageal doppler-echo study

The transoesophageal doppler-echo study was performed using an ATL 5000 HDI (Bothell, WA, USA) with a multiplane 5 MHz transducer.

Pulmonary vein stenosis was defined as follows:

1. a maximum pulmonary vein doppler flow velocity of ≥110 cm/s corresponding to data published by Yu et al. and
2. the presence of turbulence and deformity of the flow signal as defined by a minimal flow (V) between systolic (S) and diastolic (D) peak flow of ≥60% of the mean of both peaks: V≥0.6×(S+D)/2.

Transoesophageal doppler-echo and magnetic resonance imaging studies were evaluated blindly and
independently. Pulmonary vein stenosis was diagnosed if respective criteria were met in at least one of the methods. A stenosis was classified as ostial if the stenosis was located <10 mm from the ostium and as distal if the stenosis was ≥10 mm from the ostium or if the stenosis was found after the first branching.

If a pulmonary vein stenosis was diagnosed at the 2-year follow-up, repeated evaluation by transoesophageal doppler-echo and angio magnetic resonance imaging was performed 3–6 months later.

Statistical analysis

Parametric data are presented as mean±SD. The unpaired t-test was used to compare continuous variables between patients with and without pulmonary vein stenosis and Chi-square test with Yates’ correction or Fisher’s exact test was used to analyse nonparametric data. Statistical significance was defined as p≤0.05.

Results

Patients and clinical outcome

Mean age of the patients was 55±10 years, and 37 patients were males. Thirty-six patients had a history of drug resistant paroxysmal, and 11 had persistent atrial fibrillation. Thirty-nine patients had no structural heart disease.

Twenty-six patients (55%) had recurrence of atrial fibrillation during the first 4 weeks, four patients at 1–12 months and only two patients more than 1 year after the first procedure. Four patients had spontaneous late cure after early recurrences of atrial fibrillation during the first weeks after ablation and five patients were free from atrial fibrillation after a second ablation procedure.

At 2 years follow-up, 24 (51%) patients were in a stable sinus rhythm (no symptoms of atrial fibrillation and no atrial fibrillation on 24 h holter monitoring) without antiarrhythmic drugs. An additional 12 patients (26%) were free from atrial fibrillation on previously ineffective antiarrhythmic drug therapy. The success rate was higher in patients with paroxysmal atrial fibrillation: 22/36 (61%) were free from atrial fibrillation without antiarrhythmic drugs, whereas only 2/11 (18%) were with persistent atrial fibrillation.

Electrophysiologic study and ablation procedure

A total of 101 pulmonary veins (left upper pulmonary vein 35, right upper pulmonary vein 36, left lower pulmonary vein 21, right lower pulmonary vein 9) were treated. A focal pulmonary vein trigger ablation was performed in 10 patients (18 pulmonary veins), an ostial pulmonary vein isolation ablation was performed in 25 patients (69 pulmonary veins) and a combined approach in 12 patients (14 pulmonary veins). Foci outside the pulmonary veins were ablated in eight patients: right atrium three, superior vena cava two, left atrium four.

An average of 1.6 procedures/patient was performed. During the repeated procedures the following causes for atrial fibrillation recurrence were identified: additional arrhythmogenic pulmonary veins N=12, recovery of pulmonary vein conduction N=9, ostial foci N=6, left atrial foci N=3 and no foci identified N=6.

The mean duration for all procedures per patient was 353±141 min and total mean fluoroscopy time was 62±29 min. One pericardial tamponade occurred as acute complication of the procedure. Postablation pulmonary vein angiography showed five stenoses (>50%) in four patients.

Transoesophageal doppler-echo and magnetic resonance imaging

In 44 of the 47 patients, a transoesophageal doppler-echo was performed, while magnetic resonance imaging was performed in 39 patients. Three patients refused the transoesophageal doppler-echo and eight patients had a pacemaker. All four pulmonary veins could be visualised with transoesophageal doppler-echo in all but one patient in whom the left inferior pulmonary vein was not found. Complete occlusion of five pulmonary veins was present in five patients. Significant pulmonary vein narrowing was seen in 11 pulmonary veins (nine patients) (Fig. 1).

Thirty-six patients (143 veins) were examined by transoesophageal doppler-echo and magnetic resonance imaging. Of these 143 pulmonary veins, 11 stenoses were revealed by transoesophageal doppler-echo and nine of them were confirmed by angio magnetic resonance imaging. One stenosis considered to be significant by transoesophageal doppler-echo was only a 30% stenosis on magnetic resonance imaging; one stenosis was not seen by magnetic resonance imaging due to artefacts. The remaining 132 veins showed no stenosis with both methods.

The pulmonary vein stenosis/occlusion could be localised by magnetic resonance imaging and/or transoesophageal doppler-echo in 14 of 16 stenoses/occlusions (Fig. 2). The remaining two stenoses were only detected by transoesophageal
doppler-echo (Fig. 3) and an exact localisation was not possible. This may be due to a distal localisation of the stenosis in a small branch producing a high velocity doppler jet. Four of these 14 stenoses/occlusions were <10 mm from the pulmonary vein ostium and the remaining 10 stenoses were >10 mm with a maximum distance of 51 mm (Fig. 1).

An ablation site of more than 10 mm from the ostium was associated with a 5.6-fold higher risk of pulmonary vein stenosis than an ostial ablation site (Table 1). A clear relationship was observed between the vein diameter and the incidence of stenosis: diameter of ablated pulmonary vein without stenosis was 13.0±3.1 mm and that with stenosis 10.4±5.5 mm, \( p \leq 0.05 \). On the other hand, there was no correlation between the development of stenosis and clinical data (age, gender) and ablation specific parameters (total ablation duration, total radiofrequency power).

One patient with two stenoses of the upper pulmonary veins detected by angiography during the initial procedure (Fig. 4A) underwent transoesophageal doppler-echo and magnetic resonance imaging 3, 6, 12, 15 and 24 months later. A progression to complete occlusion of the left upper pulmonary vein was found at 12 months and that of the right upper pulmonary vein at 15 months (Fig. 4B). Two of the three patients with occlusion of one PV at the 24-month follow-up had a moderate stenosis detected by angiography at the end of the electrophysiological study. In one patient, the angiography of the later occluded vein had not been performed due to technical problems. No change of stenosis was noted in the remaining patients 4.3±1.1 months after the 2-year follow-up.

Only three of 13 patients with pulmonary vein stenosis complained of moderate dyspnoea on exertion, the remaining 10 patients did not report any symptoms. Two of the symptomatic patients had stenosis or occlusion of two pulmonary veins. None of these symptomatic patients had an organic heart disease or an abnormal transthoracic echocardiogram. However, they had elevated pulmonary wedge pressure at 75–100 W and mismatch on the ventilation/perfusion lung scintigraphy. No
intervention has yet been performed in these patients.

Discussion

To the best of our knowledge, this is the first systematic surveillance on the success and the incidence of pulmonary vein stenosis after catheter ablation of refractory atrial fibrillation after a long-term follow-up of 2 years.

We show that the rate of pulmonary vein stenosis is considerably higher than suspected by clinical assessment. Only three patients had symptoms suggestive of pulmonary vein stenosis, whereas systematic surveillance by transoesophageal doppler-echo and/or angio magnetic resonance imaging revealed pulmonary vein stenosis in 13/47 (28%) patients. The high concordance with regard to transoesophageal doppler-echo and magnetic resonance imaging pulmonary vein assessment demonstrates that our definition of pulmonary vein stenosis is valid.

Complete occlusion of five pulmonary veins was noted in four patients. Significant stenosis was encountered in 11 pulmonary veins (nine patients). Only five pulmonary vein stenoses of more than 50% had been detected by angiography at the end of the ablation procedure, indicating a development and progression of stenosis during the follow-up period. Animal data have shown that pulmonary vein luminal narrowing is based on progressive intimal proliferation, collagen replacement of necrotic myocardium, endovascular contraction and proliferation of elastic lamina over the study time of 14 weeks.6

Haissaguerre et al.4 found a pulmonary vein stenosis by angiography in five patients of the 58 studied (8.6%) at 5±4 months after an ostial pulmonary vein isolation procedure. Others found a significant increase in pulmonary vein doppler flow velocity in up to 33% of treated patients after a

Table 1 Comparison of parameters in patients with stenotic and nonstenotic pulmonary veins after radiofrequency catheter ablation for atrial fibrillation

<table>
<thead>
<tr>
<th></th>
<th>Nonstenosis (n=34)</th>
<th>Stenosis (n=13)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55±11</td>
<td>55±8</td>
<td>0.91</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>26/8</td>
<td>11/2</td>
<td>0.71</td>
</tr>
<tr>
<td>Total pulse duration (s)/pulmonary vein</td>
<td>958±700</td>
<td>1050±642</td>
<td>0.68</td>
</tr>
<tr>
<td>Total power (WS)/pulmonary vein</td>
<td>22952±15578</td>
<td>28974±15192</td>
<td>0.25</td>
</tr>
<tr>
<td>Pulmonary vein diameter (mm)</td>
<td>13.0±3.1</td>
<td>10.4±5.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Ablation site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal (N=22)</td>
<td>12</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Ostial (N=37)</td>
<td>34</td>
<td>3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Fig. 3  Stenosis of the left upper pulmonary vein. Colour flow doppler shows turbulent flow (left). Guided by colour flow, pulsed wave doppler (PW) demonstrates peak flow of 200 cm/s in combination with turbulence and deformity of the systolic/diastolic flow signal (right).
mean follow-up of 7±3 months with no correlation to the ablation parameters. In this study of Yu et al. only 5% of the patients were treated by ostial radiofrequency applications. Our results may explain the different incidences of pulmonary vein stenosis reported in the above-cited reports. In our study population the risk of pulmonary vein stenosis was 3/37 (8%) with an ostial ablation site and 10/22 (45%) with a distal ablation site in smaller vessels. Other radiofrequency parameters like the total delivered power or the total ablation time per pulmonary vein were not correlated with the risk of stenosis (Table 1).

The patients studied represent our early experience between 1997 and 1999 with conventional mapping and pulmonary vein ablation technique. It remains unclear whether novel mapping strategies (circumferential 10 electrodes or basket catheter), alternate ablation energy/catheter technology (cooled radiofrequency ablation, ultrasound, cryoablation) or an anatomical ablation approach would reduce or eliminate the risk of pulmonary vein stenosis.

Nevertheless, our study clearly demonstrates that systematic surveillance by appropriate imaging modalities is needed to assess the true risk of pulmonary vein stenosis with newer ablation techniques.

**Limitations**

Three different techniques were used to visualise pulmonary veins: angiography during the electrophysiological study, angio magnetic resonance imaging and transeosophageal doppler-echo during follow-up. Thus, the real rate of pulmonary vein stenosis progression cannot be indicated because

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Fig. 4 (A) Angiogram at the end of the electrophysiological study with a severe stenosis of the left upper pulmonary vein and a moderate stenosis of the right upper vein. (B) In the same patient, complete occlusion of the left upper pulmonary vein was found at 12 months and an occlusion of the right upper pulmonary vein at 15 months. 3-D reconstruction of angio magnetic resonance imaging.
stenosis may be missed by angiography due to technical problems. Moreover, we did not perform angi magnetic resonance imaging or transoesophageal doppler-echo examination systematically during the first year after ablation, thus we cannot determine the time course of pulmonary vein stenosis development. Finally, the circumferential extent of ablation was not documented at the time of the electrophysiological study due to the difficulties in evaluating this parameter exactly without circular mapping systems.

Conclusions
1. Focal ablations inside pulmonary veins should be strictly avoided because they are associated with a 5.6-fold higher risk of stenosis than ostial ablations.
2. Late progression of pulmonary vein stenosis to complete occlusion can occur.
3. Most patients with pulmonary vein stenosis are asymptomatic. In consequence, long-term follow-up examination of pulmonary vein patency by angi magnetic resonance imaging or by transoesophageal doppler-echo of all patients after pulmonary vein ablation is necessary.

References