

# Pulmonary Veins Isolation to Treat Patients with Refractory Paroxysmal Atrial Fibrillation. Clinical Results After a Single Procedure

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**Objective** - The purpose of this study was to assess the clinical outcome of patients submitted to a single procedure of radiofrequency pulmonary veins (PV) isolation to treat refractory paroxysmal atrial fibrillation (AF).

**Methods** - This study included 49 consecutive patients (36 male; mean age  $54 \pm 10$  years old) who had frequent symptomatic paroxysmal AF refractory to at least three antiarrhythmic drugs. We used a circular decapolar catheter for mapping PVs - left atrial connections and a 4-mm distal tip catheter for ablation (30 W and 50 C), aiming to achieve electrical isolation of 3-4 PVs.

**Results** - Twenty-five patients (51%) did not present any AF recurrence in a mean follow-up of  $12 \pm 5$  months. Twenty-four (49%) had at least one recurrence during outcome; twenty (83%) of them within the first month after the procedure and four after two to nine months. After introducing antiarrhythmic drugs 15 (63%) patients were under control, 10 were asymptomatic and five complained of sporadic short duration AF episodes. Nine (37%) patients remained very symptomatic despite the use of antiarrhythmic drugs and were referred to a new procedure of PV isolation. No patient presented major complications. At the end of the follow-up, 35 (71%) patients remained in stable sinus rhythm with no AF recurrences after a single procedure, 50% of them without antiarrhythmic drugs.

**Conclusion** - Most patients who present symptomatic paroxysmal AF refractory to antiarrhythmic drugs obtain a good clinical control after a single PV isolation procedure.

**Key words:** atrial fibrillation, radiofrequency catheter ablation, pulmonary veins

Radiofrequency (RF) ablation of ectopic beats from pulmonary veins that trigger atrial fibrillation has been recently introduced in the clinical practice<sup>1,2</sup>. Although effective, this technique can only be used for few patients who present quite active foci, which allow electrophysiological mapping and precise localization<sup>3-5</sup>. The strategy for patients with focal atrial fibrillation without active foci during electrophysiological mapping was to apply provocative maneuvers to induce their activity<sup>6</sup>. Using this strategy patients presented frequent recurrences, as many ectopic foci were present in other veins not identified in the first study<sup>7</sup>. Therefore, the empirical isolation of the four pulmonary veins has been suggested as the most effective method to treat those patients<sup>8-10</sup>. However, there are some controversies about the clinical results and necessity of new procedures to obtain a good clinical control of these patients<sup>11,14</sup>. The aim of this study was to assess the clinical results obtained from patients with refractory paroxysmal atrial fibrillation submitted to a single radiofrequency procedure to empirically isolate three or four pulmonary veins.

## Methods

From January 2001 to August 2002, forty-nine consecutive patients were prospectively studied. They presented refractory paroxysmal atrial fibrillation and were referred to radiofrequency catheter ablation, aiming to empirically isolate pulmonary veins of the left atrium. Thirty-six men and 13 women, mean age of  $54 \pm 10$  years old (32 to 76 y.o.) presenting atrial fibrillation for more than two years and having unsuccessfully used at least three antiarrhythmic drugs before considering atrial fibrillation ablation were included in this study. Patients presenting frequent atrial premature contractions (APC) or atrial tachycardia triggering atrial fibrillation during the electrophysiological mapping were excluded. In those patients the procedures were referred for specific foci mapping and focal ablation. Atrial fibrillation was regarded

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paroxysmal when episodes were spontaneously reverted before 48 hs. Patients submitted to electrical (ECV) or chemical (CCV) cardioversion were enrolled in this study if ECV or CCV were performed within a period of 48 hs from the beginning of the crises. Among 49 patients, five presented chronic coronary disease (two with previous myocardial infarction); one presented mild dilated cardiomyopathy; one asymmetric hypertrophic cardiomyopathy and the others did not present structural heart disease. Seven patients had systemic arterial hypertension under clinical control. The mean left atrium size was  $40 \pm 6$  mm (29 to 50 mm). Patients underwent oral anticoagulation from four to six weeks (RNI between 2.5 and 3.5) or performed transesophageal echocardiography within 24 hs to assure there was not any atrial thrombus before the procedure. Pulmonary magnetic resonance angiography (MRI) with Gadolinium was suggested but not mandatory to perform the study.

Patients were taken to the electrophysiologic room after 8 hs of fasting state, and sedated with intravenous propofol. Arterial blood pressure, digital oximetry and  $\text{CO}_2$  exhaled were non-invasively monitored. Three multipolar electrode catheters were inserted into the femoral vein and placed under fluoroscopy guidance. One 6 F decapolar catheter was inserted into the coronary sinus; one 6 F circular decapolar ("Lasso" – J&J) catheter was introduced by a long sheath in the left atrium through the foramen oval or by transeptal puncture. One 7 F or 8 F (EPT or J&J) regular catheter for RF ablation with a 4-mm distal tip electrode was also introduced in the left atrium by a second transeptal puncture if necessary. Heparin was infused (10.000 IU) and the activated coagulation time (ACT) was evaluated after 15 minutes, repeated each hour, aiming to maintain ACT between 250 and 350 seconds. Pulmonary veins angiography was performed with Meglumine loxalate (32,5 g/100ml) using one of the long transeptal sheaths, except for the right inferior pulmonary vein that was not systematically evaluated. The pulsed fluoroscopic images in a 7 square / second were obtained (Fisher system) in the left anterior oblique position ( $40^\circ$ ) for the left pulmonary veins and in the right anterior oblique position ( $30^\circ$ ) for the right pulmonary veins. In this system the fluoroscopic time measurement is restricted to X-ray pulsed-time<sup>15</sup>. Electrophysiologic data were digitally recorded by a PC Electrophysiologic Measurement System (EMS 4.2 – University of Limburg - The Netherlands).

The pulmonary veins isolation technique consisted in mapping the left veno-atrial junction using the "Lasso" catheter to localize pulmonary veins in connection with the left atrium and disconnect them by applying RF pulse of 30 W and  $50^\circ$  C from 30 to 60 seconds. The "Lasso" decapolar catheter was introduced in the pulmonary vein after angiography and then removed until being nearly five mm of the ostium (Figure 1). Pulmonary vein isolation was performed if potentials were present. The vein isolation criterion was the disappearance of electrical potentials in the vein during sinus rhythm or continuous atrial stimulation (entrance block) (Figure 2). The isolation of such veins was performed under continuous electrical stimulation of the distal

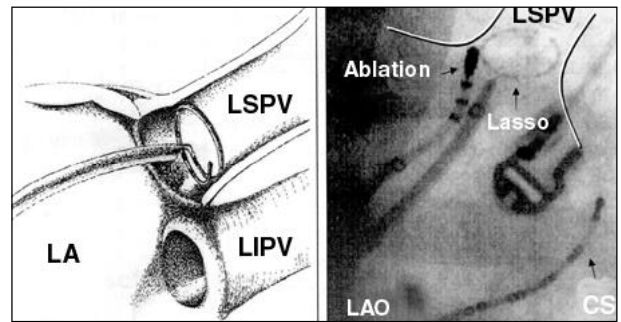


Figure 1 - Pulmonary vein isolation technique to treat paroxysmal atrial fibrillation. A) Representation of catheter position in the left superior pulmonary vein ostium (LSPV). B) Left anterior oblique (LAO) fluoroscopic projection during LSPV isolation. Note radiofrequency ablation catheter at the LSPV ostium. LA - left atrium; LIPV - left inferior pulmonary vein; CS - coronary sinus catheter.

coronary sinus in order to distinguish left vein potentials from left atrial appendage electrograms. The right pulmonary veins were mapped during sinus rhythm with no atrial stimulation. RF ablation was initially directed towards the most suggestive point regarding the atrial vein connection localization and kept for 30 s. Conduction block through the veno-atrial connection was shown by conduction delay in this specific sector and by the change in activation sequence of the ostium analyzed by the circular catheter activation (figure 2). Applications were repeated in other connection points until complete isolation of pulmonary vein was obtained. After 10 to 12 pulses sequence, we performed evaluation of the pulmonary vein permeability by angiography with contrast. Applications were stopped when there was reduction of vein ostium size or still due to the amount of applications, initially and empirically established around 20 to 25 applications. Pulmonary vein isolation was complete when all venous potentials obtained from the circular catheter disappeared. However, when amplitude of such potentials was reduced but with no complete disappearance, we considered pulmonary vein connections just as partially modified. After the end of the procedure, infusion of 10 to 40 micrograms of isoproterenol was performed followed by 12 to 18 mg of adenosine, in order to identify ectopic triggers outside the veins. Patients were kept in resting position during 4 hours and in general discharged the day after. Subcutaneous low molecular weight heparin (1 mg/Kg/ twice a day) was started six hours after the end of the procedure and maintained until oral coagulation was obtained (INR 2.5 to 3.5). Antiarrhythmic maintenance depended on symptoms recurrence within the first 24 hours or on the discomfort intensity provoked by atrial fibrillation crises before ablation.

Clinical follow-up was performed according to clinical appointments in our institution, or still by telephone contact with patients unable to come personally. Patients with pulmonary vein stenosis suspicion were evaluated by pulmonary vein angiography, transesophageal echo or pulmonary ventilation/perfusion cintigraphy one to six months after the procedure. Patients were clinically evaluated in one month and each three months. In case of recurrence, we suggested EKG documentation of the crise. Ambulatorial

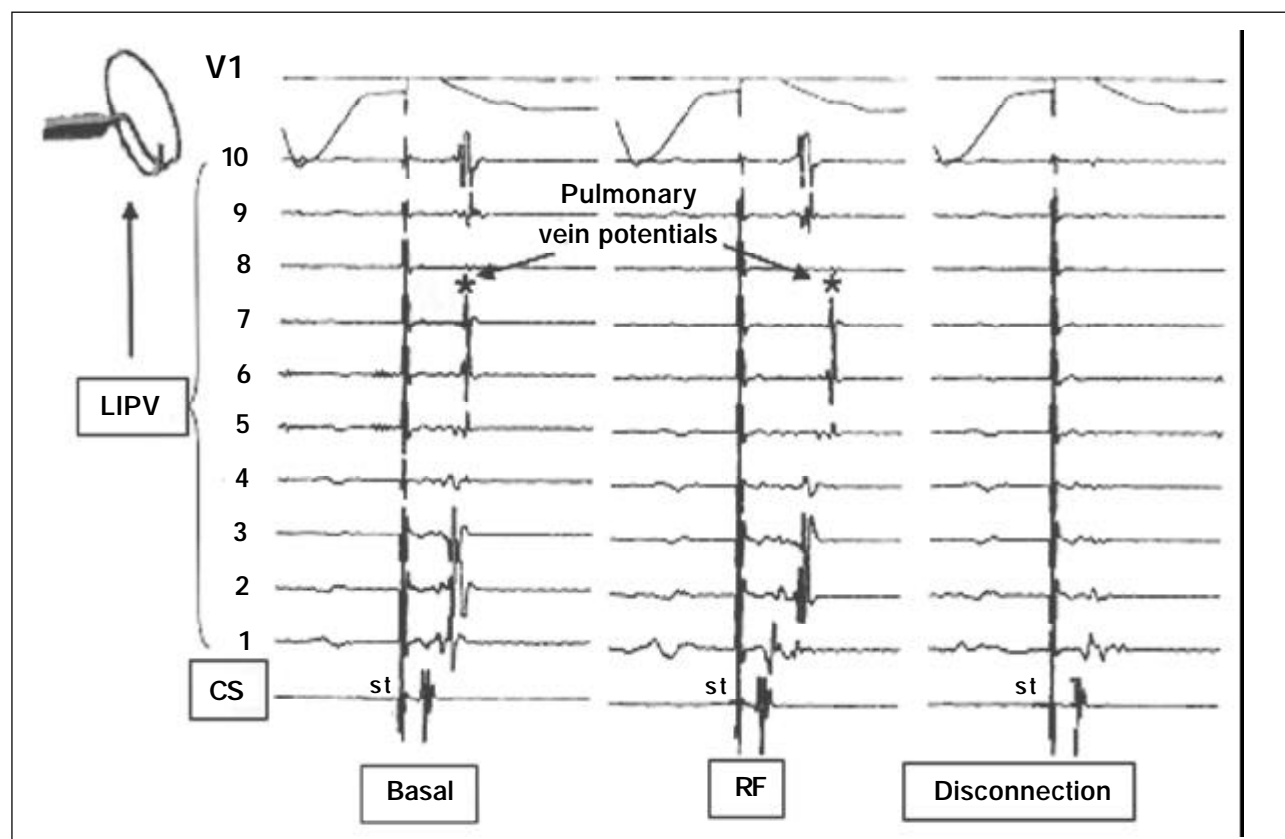


Fig. 2 - Left inferior pulmonary vein (LIPV) isolation. Basal: Pulmonary vein electrograms from 1 (distal) to 10 (proximal) obtained by the circular ("Lasso") catheter positioned in the LIPV ostium during atrial pacing (st) in distal coronary sinus (CS). RF: Note the "Lasso" catheter electrogram activation changing during radiofrequency (RF) application secondary to entrance conduction block in a sector of the LIPV ostia. Disconnection: LIPV isolation. Observe that pulmonary vein potentials obtained by "Lasso" catheter disappeared. CS pacing activates the left atrium, but it does not achieve the interior of LIPV.

monitoring (Holter and symptomatic events recordings) was used to clarify suggestive symptoms of atrial fibrillation recurrence not documented in EKG. Typical symptoms of atrial fibrillation recurrence were accepted in the absence of EKG documentation.

As Statistical Analysis we used the Student *t*-test to compare continuous variables and the Fisher test to compare proportions. We considered 5% a significant statistical level.

## Results

We performed ostial radiofrequency ablation in 184 veins (49 patients - 3.7 veins per patient). A mean of  $21 \pm 12$  RF pulses per vein was applied in each patient:  $25 \pm 14$  at the left superior pulmonary vein (LSPV) ostium;  $22 \pm 10$  at the right superior pulmonary vein (RSPV);  $13 \pm 9$  at the left inferior pulmonary vein (LIPV) and  $23 \pm 12$  at the right inferior pulmonary vein (RIPV). Procedure mean time and X ray time exposition were  $231 \pm 47$  min and  $12 \pm 4$  min, respectively. Complete isolation was obtained in 146 out 184 (79%) veins, 40 LSPV (82%), 41 RSPV (84%), 35 (81%) and 30 of 45 RIPV (67%). All four pulmonary veins were completely isolated in 18 patients; three veins in 20 patients; two veins in six; one vein in three and two patients did not have any vein comple-

tely isolated. In those cases, just the ostium electrogram amplitude reduction was obtained.

Patients did not present any important complication during hospitalization and follow-up. No patient presented important hematoma or vascular complication. There were no complications related to transeptal puncture, pulmonary vein stenosis or embolic events.

After ablation, 25 patients (51%) did not present recurrence in a mean follow-up of  $12 \pm 5$  months. Of those, 22 (88%) had three or four pulmonary veins isolated and three (12%) had two or less veins isolated. Nineteen patients remained asymptomatic and six complained of palpitations related to premature contractions. Fifteen (60%) patients were not using antiarrhythmic drugs; four (16%) were using beta-blockers, three due to systemic arterial hypertension and one due to premature ectopic beats perception; and six (24%) were under amiodarone.

Twenty-four (49%) patients presented at least one recurrence during follow-up; in 20 (83%) recurrence occurred within the first month after RF ablation, and in four (17%) after two to nine months of follow-up (figure 3). After introducing antiarrhythmic drugs (beta-blockers: six, amiodarone: six, sotalol: three, propafenone: two, flecainide: one and diltiazem: one), fifteen (63%) patients presented important symptoms relief, ten became asymptomatic (including four

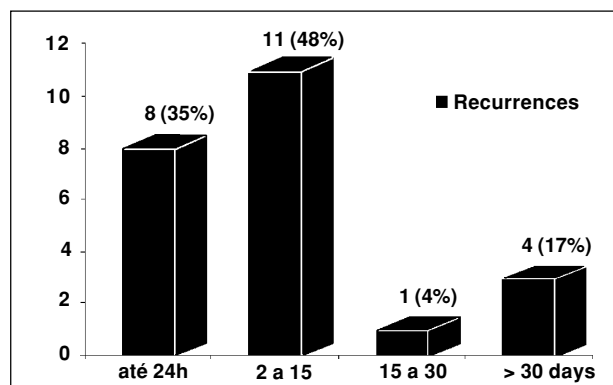


Figure 3 - Atrial fibrillation recurrence rate after pulmonary vein isolation. Observe that 19 (82%) of 23 recurrences occurred in the first 15 days after the procedure.

patients who stopped drugs) and five referred sporadic and short AF episodes. Nine (37%) remained with symptoms unchanged despite the use of antiarrhythmic drugs and seven were submitted to a second procedure. At the end of the follow-up, 35 (71%) of the patients remained in stable sinus rhythm without atrial fibrillation recurrences after a single procedure. No patient presented symptoms related to systemic emboli or pulmonary veins stenosis.

## Discussion

The electrophysiologic observation that atrial fibrillation is triggered by ectopic foci frequently originated in the pulmonary veins opened a new era in radiofrequency catheter ablation. However, just few patients presented frequent spontaneous ectopic beats enough to allow mapping of specific foci<sup>2-5</sup>. The attempts to apply the potential clinical benefits of AF triggers by catheter ablation presented major limitations. Difficulty to localize all ectopic foci which triggered atrial fibrillation and low reproducibility of the provocative maneuvers to induce the triggers resulting in high AF recurrence rate after ablation, consequently, many ablation procedures were necessary to obtain good clinical control<sup>6-8</sup>. Additionally, multiples radiofrequency pulses applied in the ostium of pulmonary veins may cause pulmonary vein stenosis, sometimes resulting in severe pulmonary hypertension<sup>16-17</sup>. Aiming to solve these problems two strategies were developed in order to isolate the four pulmonary veins in a single procedure with low risk of pulmonary veins stenosis: mapping and ablating specific sectors of pulmonary veins ostia<sup>8,9</sup> and circumferential ablation of pulmonary veins ostia using a 3-D electro-anatomic system<sup>10,11</sup>.

The pulmonary vein isolation technique developed by Haissaguerre et al aims to electrically isolate pulmonary veins minimizing the stenosis risk<sup>8,9</sup>. It is based on recognizing veno-atrial junction connections by the circular catheter positioned at the pulmonary veins ostia<sup>18,19</sup>. Through the use of this technique, radiofrequency applications can be optimized and the stenosis risk lower. Haisaguerre et al, reported 3% of symptomatic pulmonary veins stenosis<sup>9</sup>. Oral et al, applying the same technique did not report pulmo-

nary veins complications<sup>12</sup>. Marrouche et al, reported pulmonary vein stenosis during high energy radiofrequency application inside the veins through irrigated tip catheters. Pulmonary vein stenosis were not observed after using intracardiac echocardiogram to adequate radiofrequency applications<sup>13</sup>. In this study we did not observe any manifestation related to pulmonary veins stenosis. However, clinical manifestation occurs just when the pulmonary vein stenosis is very important, mainly when there is more than one vein involved<sup>16,17</sup>. Symptoms, in general, occur in the first days after the procedure, but can occur later<sup>20</sup>. In this study, we did not evaluate pulmonary veins systematically during follow-up, however all patients but one were followed for more than six months and none of them reported any symptom related to pulmonary veins stenosis. These initial data confirm other observations suggesting that ablation of pulmonary vein ostia applying low energy radiofrequency pulses presents low risk of promoting pulmonary vein stenosis. Nevertheless, further studies are necessary to confirm the safety of this procedure.

There are some controversies related to the clinical results of pulmonary veins isolation to treat patients with recurrent atrial fibrillation. Stable sinus rhythm without atrial fibrillation recurrence has been reported from 70% to 94%<sup>11-14,21</sup>. This success rate variation can be related to patients selection, pulmonary veins isolation technique, number of procedures applied, antiarrhythmic drugs used and patient's follow-up<sup>22</sup>. Ectopic foci located outside the pulmonary vein ostia or related to other atrial structures have been described as a cause of atrial fibrillation recurrence after pulmonary veins isolation<sup>23,24</sup>. In our study, some patients without complete PV isolation had also good clinical evolution and radiofrequency applications around the pulmonary veins ostia could be responsible for that. Those lesions applied around the pulmonary veins ostia could ablate focal triggers of atrial fibrillation and could explain why two of our patients without any PV completely isolated became free of atrial fibrillation recurrence, one of them without antiarrhythmic drugs. Pappone et al, have systematically applied RF lesions around the four pulmonary veins. Although pulmonary veins isolation was obtained in just 75% of all patients, 85% of them did not present atrial fibrillation, most of them without antiarrhythmic drugs<sup>10,11</sup>. However, reconnection of pulmonary vein previously isolated seems to be the most common cause of recurrence and obtaining a definitive, without increasing the pulmonary veins stenosis risk is one of the technical challenges to be solved. Marrouche et al has suggested that performing deep lesions outside the vein through an 8-mm tip catheter is related to better results<sup>13</sup>. However, Macle et al, using a 4-mm irrigated tip had to perform two or three procedures in 49% of patients obtaining clinical control in 80% of them, 44% using antiarrhythmic drugs<sup>14</sup>.

In this study 47% of our patients presented at least one recurrence after pulmonary veins isolation. In most of them recurrences occurred within two weeks after radiofrequency ablation. But, after the first month they became asymptomatic or oligosymptomatic after antiarrhythmic introduction. This observation was also reported by other

authors<sup>13,25</sup>. The radiofrequency lesion repair process could be responsible for this evolution<sup>13</sup>. Otherwise, an inflammatory process induced by radiofrequency lesions on the pulmonary veins ostia could induce atrial fibrillation transitory episodes. Such observations were reported by other authors that suggested to perform a new intervention for pulmonary vein isolation just after six or eight weeks of the first procedure<sup>11, 14</sup>. Postponing a new intervention for 4 to 6 weeks and restricting it to symptomatic patients non con-

trolled by antiarrhythmic drugs we indicated a new procedure just for 16% of our patients.

In summary, most patients presenting refractory paroxysmal atrial fibrillation obtain a good clinical control after a single procedure of empirical isolation of four pulmonary veins. Atrial fibrillation recurrences, when occur, are more frequent in first two weeks after the procedure, but, in most patients it is possible to obtain a good clinical control during outcome.

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