

Transesophageal echocardiographic follow-up of pulmonary veins in patients undergoing ostial radiofrequency catheter ablation for atrial fibrillation

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Key words:

Atrial fibrillation;
Catheter ablation;
Pulmonary vein stenosis;
Transesophageal echocardiography.

Background. Ostial radiofrequency catheter ablation (RFCA) of pulmonary veins (PVs) is a promising invasive approach for the non-pharmacologic treatment of atrial fibrillation, but PV stenosis has been reported as a possible complication of this intervention. The aim of this study was to assess PV anatomy and stenosis (i.e. number and progression) by means of transesophageal echocardiography (TEE) during the follow-up of patients undergoing RFCA.

Methods. Twenty-three consecutive patients with refractory and highly symptomatic atrial fibrillation underwent ostial radiofrequency isolation of arrhythmogenic triggers/foci, localized into the PVs, by an electroanatomic approach (CARTO system) or circular mapping with a multipolar catheter (LASSO) placed under radioscopy guidance. All patients were investigated using TEE and magnetic resonance angiography before radiofrequency application to evaluate PV anatomy. TEE examination was repeated after 2 months of follow-up and, in the presence of a stenosis, 1 year later.

Results. TEE allowed to identify 100% of the left and right superior PVs, 96% of right inferior PVs, and 74% of the left inferior PVs. Anatomic variants were detected at TEE in 33% of patients against 37% at magnetic resonance angiography (95% of concordance). After ostial RFCA, TEE disclosed a significant reduction in the mean diameters of the left superior PV (14.1 ± 3.2 vs 12.0 ± 2.7 mm, $p < 0.01$), left inferior PV (11.2 ± 2.3 vs 9.8 ± 2.2 mm, $p = 0.05$) and right superior PV (14.2 ± 2.6 vs 12.9 ± 2.7 mm, $p < 0.05$), and an increase in the mean peak velocities of the left superior PV (69.8 ± 14.8 vs 91 ± 42.4 cm/s, $p < 0.05$) and left inferior PV (59.2 ± 18.1 vs 79.3 ± 40.5 cm/s, $p < 0.05$). From a total of 88 PVs treated, 7 (7.9%) showed a higher significant stenosis in patients treated using the LASSO than the CARTO system (31.3 vs 2.8% respectively, $p < 0.01$). After 1-year follow-up there was no progression of PV stenosis.

Conclusions. TEE was successful to evaluate PV anatomy and stenosis of patients undergoing ostial RFCA for atrial fibrillation. This complication is not rare and seems to be strictly related to the method of ablation, in particular when circular mapping and disconnection of triggers/foci was carried out by only a circular multipolar catheter without an electroanatomic approach.

(Ital Heart J 2005; 6 (7): 595-600)

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Received November 17, 2004; revision received February 2, 2005; accepted February 4, 2005.

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Atrial fibrillation is the most common arrhythmia and its prevalence in the general population reaches 0.4%, increasing with age up to 8-16% in the elderly¹⁻³. Recent researches have demonstrated a focal origin of this disorder and the important role played by the pulmonary veins (PVs) as a trigger of atrial fibrillation⁴⁻⁸.

Radiofrequency catheter isolation of the triggers-sleeves of myocardial tissue, localized into the PVs, has been reported to be effective in preventing recurrences of atrial fibrillation⁹⁻¹² and reducing the risk of PV stenosis¹³⁻¹⁸.

In previous studies pulmonary angiography, computed tomography (CT) or magnetic resonance angiography (MRA) were

usually employed to reveal PV anatomy and to study the progression of pulmonary stenosis after radiofrequency delivery near the PV ostia^{14,16,19-26}.

The aim of this study was to assess PV anatomy/stenosis and, consequently, to follow up these patients by means of transesophageal echocardiography (TEE).

Methods

Study population. From July 2001 to November 2003, 23 consecutive patients (22 males, 1 female, mean age 56.2 ± 7.6 years) with symptomatic, drug-refractory atrial fibrillation (mean duration 3.9 ± 3.2 years)

underwent radiofrequency PV isolation. Ten patients (43.0%) were on antihypertensive treatment and 1 (4.3%) had a coronary artery disease, but all had preserved left ventricular systolic function assessed at transthoracic echocardiography. All were treated with oral anticoagulants maintaining the international normalized ratio (INR) between 2 to 3. A TEE was performed 1 week before PV disconnection to exclude the presence of atrial thrombi and examine the PVs. Another TEE was repeated 2 months after ablation.

A gadolinium-enhanced MRA with a 1.5-T magnetic resonance imaging system was performed 1 month before the first TEE and ostial radiofrequency catheter ablation (RFCA) to define PV anatomy.

All subjects were followed up by 24-hour ECG monitoring, clinical evaluation and transthoracic echocardiography at 3, 6 and 12 months of follow-up.

Ablation procedure. Briefly, after having obtained written informed consent, all patients underwent an electrophysiologic study and radiofrequency catheter disconnection of the PVs, while maintaining pharmacologic therapy. All patients were also treated with an intravenous bolus of unfractionated heparin (70 U/kg). PV isolation was achieved by means of the following two strategies: a) electroanatomic mapping of the left atrium (18 patients) using the CARTO system (Biosense Webster, Diamond Bar, CA, USA) with radiofrequency delivery applied following circumferential lines around the PV ostia; b) for distal isolation guided by circular mapping, a multipolar circular catheter (LASSO, Biosense Webster, Diamond Bar, CA, USA) was placed in a stable position inside or at the ostial level of the PVs under radioscopy guidance (5 patients) and isolation was attempted by targeting recording to PV potentials since their complete disappearance.

Radiofrequency delivery was provided by an ablation 5-mm irrigated-tip catheter (NaviStar, Biosense Webster, Diamond Bar, CA, USA), and energy settings were 30 W for the superior PVs and right inferior PVs (RIPVs), and 20 W for the left inferior PVs (LIPVs). The delivery duration was 30-60 s for each site in a temperature-controlled mode with a maximum temperature of 50°C.

Target of both types of procedures was the disappearance of PV potentials inside each PV.

After RFCA, heparin infusion was continued for 48 hours to maintain a partial thromboplastin time of 60-90 s and oral anticoagulation, discontinued 2 days before, was restarted (to obtain an INR of 2 to 3) and administered for at least 3 months.

Transesophageal Doppler echocardiographic study.

TEE was performed 1 week before and 2 months after RFCA using an Omni-1 multiplane transducer linked to an HP Sonos 5500 ultrasound machine (Philips Medical System, Andover, MA, USA). It was performed with all patients in postabsorptive state by topical anes-

thesia of 4% lidocaine spray. They were always placed on the left lateral decubitus position and an ultrasound probe was advanced to approximately 30-35 cm from the incisors. Both atria and left atrial appendage were explored to exclude the presence of thrombi or spontaneous echocontrast. The left superior and inferior PVs were seen at 0-90° and the transducer was rotated counterclockwise. The best images of the right PVs were obtained by keeping an angle of 0-45° but the transducer was rotated clockwise. Color Doppler examination was applied to obtain the best images of the PVs and to guide the continuous wave Doppler and the pulsed wave Doppler placement on the superior and inferior PVs respectively, the last one used only when an optimal alignment of continuous wave Doppler was not achieved. However, a sampling volume was placed into the PVs, 1 cm from the PV-left atrial junction and continuous wave Doppler was employed to confirm the peak flow velocity.

An increase in flow velocity was defined as a peak flow velocity ≥ 110 and < 150 cm/s, whereas a significant stenosis (i.e. lumen narrowing $\geq 70\%$) was defined as a peak flow velocity ≥ 150 cm/s and at least 2 times greater than baseline.

PV diameters were measured in three consecutive cardiac cycles using an electronic caliper by including the superior endothelial edge and excluding the inferior one.

All data were recorded on videotape and/or magneto-optic disk for off-line analysis being unaware of the MRA results.

When a significant PV stenosis was found, TEE was repeated after 1 year.

Statistical analysis. Continuous variables were expressed as mean \pm SD or as median values (range) if the distribution was not Gaussian. Distribution normality was assessed by the Kolmogorov-Smirnov test. A paired Student's t-test was used for comparison between groups. The Fisher's exact test was used to compare non-continuous variables. The null hypothesis was rejected for all tests with two-tailed alpha values of < 0.05 .

For determination of the interobserver and intraobserver variability, variables for 10 randomly selected patients were analyzed by two observers in a blinded fashion (interobserver variability) and by the same observer 1 week apart (intraobserver variability).

The JMP 5.01 (SAS, Cary, NC, USA) and GraphPad InStat 3.01 (GraphPad Software, San Diego, CA, USA) softwares were used for statistical analysis.

Results

In our population, triggering ectopic beats from the superior PVs were detected in 2 patients and from all PVs in 21, for a total of 88 arrhythmogenic foci.

Pulmonary vein anatomy. TEE identified a typical PV anatomy with four distinct PV ostia in 16 patients (69.6%), a left common ostium (defined as one large orifice where two veins led into) in 1 patient (4.3%), and a right middle PV in 7 (30.4%). TEE also confirmed all anatomic variants found at MRA 1 month before the procedure, but one left common ostium (95% of concordance). The superior PV ostia were identified in 100%, while RIPV and LIPV ostia in 96 and 74% of subjects, respectively.

When TEE failed to identify the LIPVs, MRA confirmed the presence of a very small ostium. The mean ostial diameters measured using TEE before catheter ablation were 14.1 ± 3.2 mm for the left superior PVs (LSPVs), 14.2 ± 2.6 mm for the right superior PVs (RSPVs), and 11.2 ± 2.3 and 11.4 ± 1.8 mm for the LIPVs and RIPVs, respectively.

The left atrial size and left atrial mechanical function^{27,28} did not show any significant change after 2 months of follow-up (Table I).

There were no differences in heart rate and body mass index at the second TEE evaluation. None of the patients suffered from a valvulopathy that could interfere with PV velocities.

Pulmonary vein stenosis. After 2 months of follow-up there was a significant narrowing of the mean LSPV and RSPV ostial diameters. Since the LIPV and RIPV diameters were narrower than before RFCA, these data were not significant for RIPVs and quite significant for LIPVs (Table II).

Moreover, we found a significant increase in mean peak flow velocities of LSPVs and LIPVs compared to baseline values and a trend toward an increase in those

Table I. Left atrial (LA) dimensions and mechanical function before and after radiofrequency catheter ablation.

	Pre-ablation	Post-ablation	p
LA area (cm ²)	20.5 ± 4.3	21.0 ± 3.2	NS
LA FAC (%)	33.8 ± 9.3	35.2 ± 7.8	NS
A wave (cm/s)	61.3 ± 13.0	57.5 ± 18.5	NS
AFF	0.36 ± 0.04	0.35 ± 0.09	NS

AFF = atrial filling fraction; FAC = fractional area change.

Table II. Pulmonary vein diameters before and after radiofrequency catheter ablation.

	Pre-ablation	Post-ablation	p
LSPV (mm)	14.1 ± 3.2	12.0 ± 2.7	<0.01
LIPV (mm)	11.2 ± 2.3	9.8 ± 2.2	0.05
RSPV (mm)	14.2 ± 2.6	12.9 ± 2.7	<0.05
RIPV (mm)	11.4 ± 1.8	10.7 ± 1.0	NS

LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

of the right PVs (Table III). According to our definition, 13 of 88 disconnected PVs (14.7%) had increased peak flow velocities (≥ 110 cm/s), and 7 (7.9%) had a significant stenosis (≥ 150 cm/s), of which 4 superior PVs, 2 LIPVs and 1 RIPV.

A total of 5 patients experienced a $\geq 70\%$ stenosis 2 months after ostial RFCA and in 2 cases this stenosis involved the two superior PVs.

Transthoracic echocardiography performed 3, 6 and 12 months after RFCA did not show pulmonary hypertension. In addition, TEE examination performed 1 year later demonstrated in 1 patient a decrease in LSPV peak velocity (from 200 to 170 cm/s).

All patients are still asymptomatic.

Table III. Pulmonary vein peak velocities before and after radiofrequency catheter ablation.

	Pre-ablation	Post-ablation	p
LSPV (cm/s)	69.8 ± 14.8	91.0 ± 42.4	<0.05
LIPV (cm/s)	59.2 ± 18.1	79.3 ± 40.5	<0.05
RSPV (cm/s)	65.7 ± 19.0	81.0 ± 36.0	NS
RIPV (cm/s)	61.6 ± 18.0	70.4 ± 33.2	NS

LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

Prediction of stenosis. All subjects received the same energy delivery (30 W in the superior PVs and 20 W in the inferior PVs) reaching the same temperature for an identical length of time.

Ten patients underwent ablation twice but just one developed PV stenosis. These data are not significant when compared to those of patients treated one time only. On the contrary, the number of stenosis was significantly higher in subjects in whom PV mapping was achieved using only the multipolar catheter approach than in those who underwent electroanatomic-guided encircling (Fig. 1).

Measurement reproducibility. The interobserver variability was $1.9 \pm 3.0\%$ for PV peak flow velocity and $5.7 \pm 3.6\%$ for PV diameter. The corresponding values for the intraobserver variability were 1.7 ± 3.1 and $5.1 \pm 3.3\%$, respectively.

Discussion

PV stenosis is a known complication of radiofrequency ablation for atrial fibrillation and many imaging modalities have been used to evaluate and follow up the PVs in such patients, especially spiral CT and MRA^{14,16,19-26}.

In the present study, the PV examination after radiofrequency catheter disconnection was assessed at

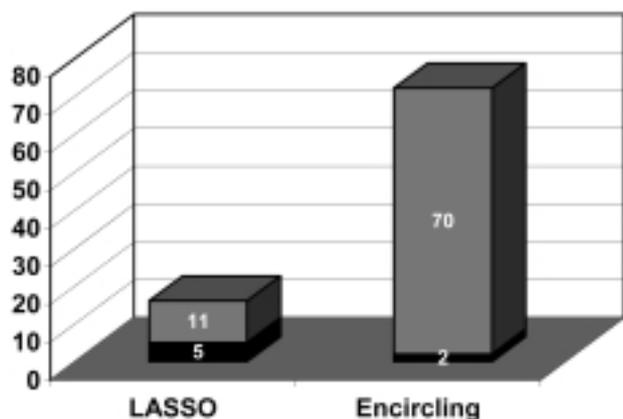


Figure 1. Comparison between radiofrequency catheter ablation performed by means of the encircling and LASSO mapping. The number of stenoses was significantly higher using the multipolar catheter mapping alone ($p < 0.01$).



Figure 2. Example of visualization of the right pulmonary veins, in particular this image shows a right middle pulmonary vein (arrow). RSPV = right superior pulmonary vein.

TEE. This technique has previously been used to examine PV stenosis of congenital etiology²⁹. TEE is a simple, minimally invasive imaging modality and it showed high reproducibility with little interobserver variability. No patient has refused this examination and under no circumstances total anesthesia was necessary.

It is important to point out that TEE sensitivity was not particularly investigated in previous published studies. Yu et al.¹⁸ used TEE to visualize only the superior PVs because of the difficulty of investigating the inferior PVs: by excluding from the study subjects with triggers/foci in these sites, TEE sensitivity was very high in the evaluation of the superior PVs. This technique has been widely used to follow up patients undergoing RFCA for atrial fibrillation, but no percentages of PV visualization are reported so far^{6,12}. Arentz et al.¹⁷ focused on TEE sensitivity to examine the inferior PVs considering that TEE was better than MRA.

In our hands TEE has well visualized the superior PVs and RIPVs, but it was sometimes difficult to highlight the LIPVs. However, it was possible to identify and follow up four PV stenoses. Moreover, TEE was also used to identify PV anatomy, in particular the sensitivity of this technique was tested for the presence of incidental anatomic variants, comparing TEE to MRA results and proving a high concordance (95%). Our finding of 34% of PV anatomic variants is consistent with prior anatomic and angiographic observations^{20,21} (Figs. 2 and 3).

The prevalence of significant stenosis (narrowing > 70%) after catheter ablation was about 8.0%, whereas the increased peak flow velocity was 14.7% (Fig. 4). In other published series the occurrence of PV stenosis ranged from 11.0 to 47.0%^{6,17}, but this percent variability probably depends upon the use of different cut-off to define a significant PV stenosis. CT scan pointed out a PV stenosis after RFCA in 3.0 to 15.6%^{13,15,19}, whereas MRA in 24.0% of cases²⁰.

CT scan and MRA are certainly more sensitive than TEE, but much more expensive with possible motion



Figure 3. Example of visualization of left pulmonary veins, in particular this image shows a left common ostium. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein.

artifacts and some variability in placement of digital caliper for measurements. Interestingly, CT scan had overestimated PV stenosis in such cases unconfirmed by successive angiographic control, still considered the gold standard method for the detection and quantification of PV stenosis^{14,15}.

We have also searched for factors that could predict PV stenosis. A significant difference between patients treated with electroanatomic encircling and those undergoing circular mapping was observed. These data are in agreement with a recent report of Saad et al.¹⁵, who analyzed five different approaches to PV disconnection and found a relationship between a high percent stenosis and distal vein isolation guided only by multipolar catheter. These data can be explained by the fact that the encircling technique provides radiofrequency delivery around the vein circumference far from the ostia, whereas with the LASSO mapping radiofrequency energy is delivered near the ostia, or in-

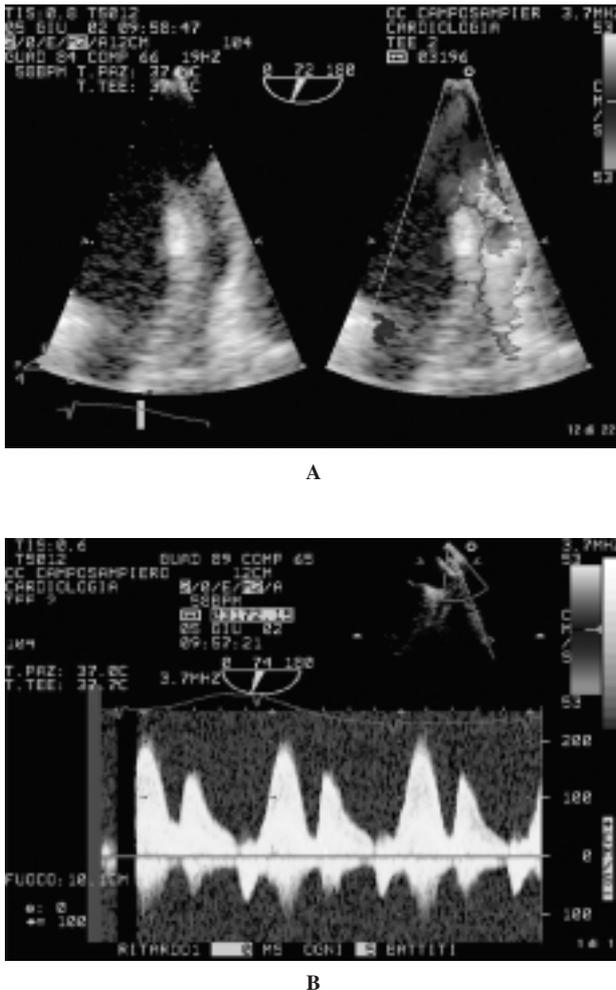


Figure 4. Image of a left superior pulmonary vein ostium narrowing (A) more highlighted by color Doppler aliasing (B). The pattern of pulmonary vein flow was normal, but a high increase in peak velocity was evidenced at continuous wave Doppler (200 cm/s).

side the PVs, causing a very proximal lesion. The risk of this complication can be minimized providing angiographic support or intracardiac echocardiography^{30,31}.

In the present study, all subjects with a significant stenosis underwent TEE follow-up 1 year after RFCA and no stenosis progressed during that time. Conversely, 1 patient showed a little regression. It is quite important to examine the state of disconnected PVs after a long period from ostial RFCA because asymptomatic progression or a new stenosis was well documented by several studies of the literature¹⁴⁻¹⁸.

PV stenosis had no clinical consequence during the 1-year follow-up. All subjects remained asymptomatic and transthoracic echocardiography did not show pulmonary hypertension. It probably depends on the fact that most of them suffered from only one PV stenosis, or two PV stenoses, both superior (i.e. draining from two different lungs). PV stenosis has been described in prior reports as an asymptomatic complication, in particular when only one vein was stenotic¹⁴. Symptoms,

such as cough, shortness of breath and hemoptysis, were also related to severe stenosis in more than one PV and, particularly, in both veins draining from the same lung^{14,15}. As a consequence, the very high sensitivity of TEE in the detection of at least three out of four PVs makes likely the identification of patients at risk of clinical complications.

In other reports, subjects with PV stenosis, even if asymptomatic, received PV balloon angioplasty because of slow lesion progression and documented occlusion during follow-up^{14,15,30,31}. Unfortunately, there was a high incidence of restenosis after PV angioplasty and follow-up was too short to achieve a conclusive judgment for this protocol^{15,24,32}. So, we preferred a conservative approach with periodical examination until symptoms of pulmonary congestion and pulmonary hypertension developed. An interesting method to distinguish patients at risk of pulmonary congestion could be stress echocardiography like in mitral valve stenosis³³.

Study limitations. The small sample size, the lack of random assignment to treatment groups and a possible influence of the learning curve might have led to an overestimation of the real rate of PV stenosis, whereas the incidence of stenosis was similar to those reported in the literature. For the same reason, the fact that all our patients remained asymptomatic should be taken into account with caution. On the other hand, the absence of an MRA control of TEE measurements was another limitation, but high costs and low availability of the former technique have refrained us from performing it twice.

In conclusion, our data suggest that TEE is feasible and able to provide either PV anatomic variants or the presence of increased peak flow velocities and significant PV stenosis after ostial RFCA for atrial fibrillation.

PV stenosis after radiofrequency ostial disconnection of PVs is not rare and it must be carefully ruled out. The risk of PV stenosis was increased when distal isolation was achieved by a multipolar mapping catheter under only radioscopic guidance, without any other viewing system. This finding is in agreement with other published observations.

Subjects suffering from PV stenosis may remain asymptomatic, but follow-up is mandatory because this complication may lead to pulmonary congestion.

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