2009

TESIS DOCTORAL

UTILIDAD DE LA RESONANCIA MAGNÉTICA EN PACIENTES CON FIBRILACIÓN AURICULAR TRIBUTARIOS DE TRATAMIENTO CON ABLACIÓN PERCUTÁNEA DE LAS VENAS PULMONARES

ROSARIO JESÚS PEREA PALAZÓN

UNIVERSITAT DE BARCELONA
Línea de investigación de biopatología cardiovascular
Dirigida por el Prof. Josep Brugada Terradellas y por la Dra. Teresa Mª de Caralt Robira

1. PRESENTACIÓN DE LOS TRABAJOS

1.1. ESTUDIO 1

Left atrial contractility is preserved after successful circumferential pulmonary vein ablation in patients with atrial fibrillation.

Perea RJ, Tamborero D, Mont L, Caralt TM, Ortiz JT, Berruezo A, Matiello M, Sitges M, Vidal B, Sánchez M, Brugada J.

***J Cardiovasc Electrophysiol*.** 2008;19:374-379

1.1.1. OBJETIVOS

Objetivo general

El objetivo general del estudio es valorar y demostrar la utilidad de la RM en pacientes con FA tributarios de APRF de las VPs.

Objetivo específico

Evaluar los cambios volumétricos y funcionales que se producen a medio plazo en la AI tras la APRF de la FA y su relación con el éxito del procedimiento.

1.1.2. RESULTADOS

De una serie de 90 pacientes consecutivos, se excluyeron 35 debido a que no se encontraban en ritmo sinusal en el momento del primer y/o segundo estudio mediante RM. Por tanto, se analizaron finalmente un total de 55 pacientes. Sus características basales se exponen en la Tabla 3.

Características de los pacientes	
Edad (años)	52.0±11.3
Sexo masculino	44 (80.0%)
Tipo de FA	
Paroxística	41 (74.5%)
Persistente	14 (25.5%)
Hipertensión	12 (21.8%)
Enfermedad cardiaca estructural	9 (16.3%)
DD VI (mm)	52.4 ± 4.7
DS VI (mm)	33.1 ± 3.8
FE VI (%)	60.0 ± 8.8
Tiempo de evolución de la FA (años)	8.4 ± 8.1

Tabla 3. Características de los pacientes
DD VI = diámetro diastólico del ventrículo izquierdo; DS VI = diámetro sistólico del ventrículo izquierdo; FE VI = Fracción de eyección ventricular izquierda. (Medidas realizadas mediante ecocardiografía antes de la ablación).

Treinta y ocho pacientes (69.1%) se mantuvieron libres de arritmia (grupo I), mientras que los 17 pacientes restantes tuvieron recurrencia de la arritmia (grupo II) tras 1.2 ± 0.3 procedimientos ablativos y durante una media de seguimiento de hasta 11.8 ± 7.2 meses (en 15 pacientes recidivó la FA y dos pacientes tuvieron flutter de nueva aparición). Entre los pacientes con ablación exitosa, 33 (60%) se mantuvieron sin tratamiento médico antiarrítmico, tres pacientes recibieron flecaidina para controlar contracciones auriculares prematuras sintomáticas, y dos pacientes se mantuvieron libres de arritmia mediante tratamiento ya sea con flecaidina o con amiodarona, que comenzaron durante el período *blanking* (período a partir de la 5ª semana después de la ablación, sin tratamiento antiarrítmico o con la utilización de un fármaco que era previamente inefectivo) y no fue interrumpido después por el facultativo de referencia.

La Tabla 4 muestra los cambios en las medidas de la AI después de la ACVP en relación al éxito del procedimiento. La Figura 16 muestra los mismos datos para cada paciente de la serie.

Tabla 4. Valores de la aurícula izquierda antes y 4-6 meses después del procedimiento ablativo

	No recurrencia de la FA (n =38)				Recurrencia de la FA (n =17)			
	Pre ACVP	Post ACVP	Disminución Media	valor *p*	Pre ACVP	Post ACVP	Disminución media	valor *p*
Vmax(ml)	98.0±19.9	84.9±17.1	13%	<0.001*	126.2±32.8	103.5±28.1	17%	<0.001*
Vmin(ml)	58.6±16.1	52.2±12.1	10%	0.004*	78.4±22.2	75.8±24.3	4%	0.315
FE AI (%)	40.2±11.5	38.1±9.8	2%	0.268	37.4±10.1	26.9±10.2	11%	<0.001*

**p* significativa < 0.05%.
Vmax = volumen máximo de la aurícula izquierda; Vmin = volumen mínimo de la aurícula izquierda; FE AI = fracción de eyección auricular izquierda; pre/post ACVP = previo/posterior a la ablación circunferencial de las venas pulmonares

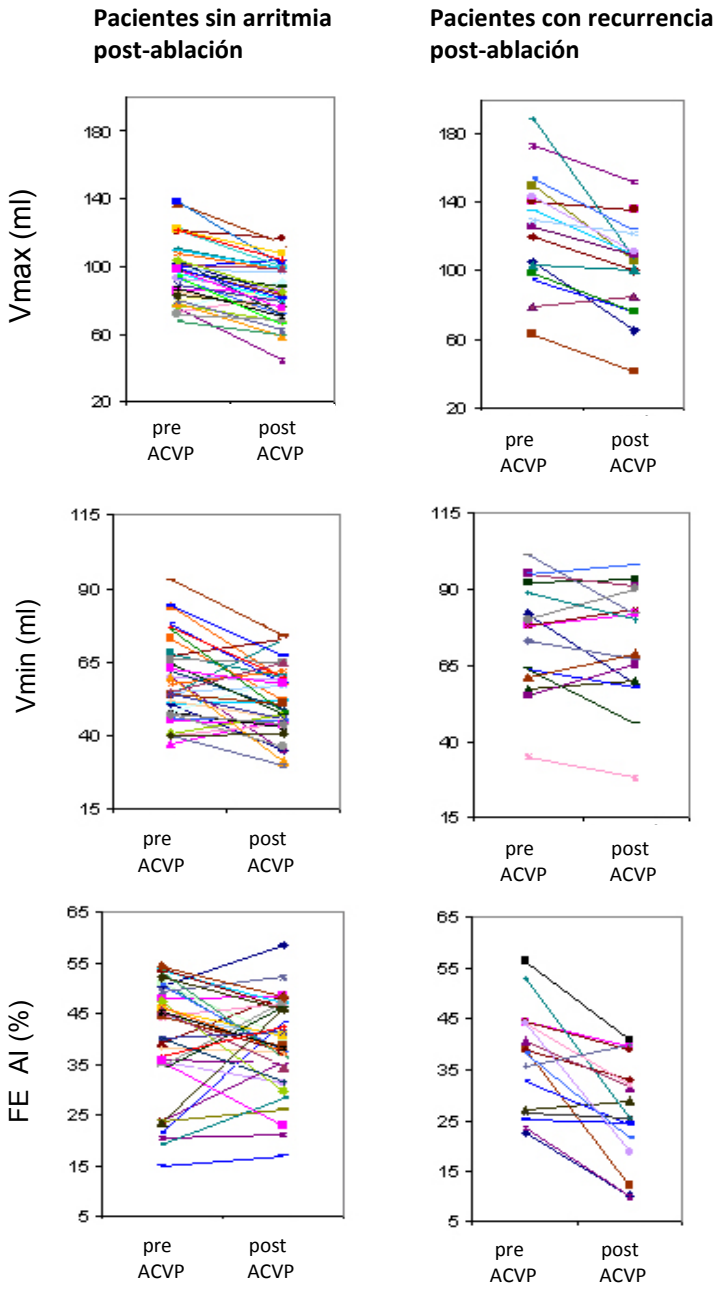

Figura 16. Evolución del volumen telediastólico de la aurícula izquierda (Vmax), volumen telesistólico de la aurícula izquierda (Vmin) y de la fracción de eyección de la AI (FE AI), 4-6 meses tras la ablación circunferencial de las venas pulmonares (ACVP) en cada paciente de la serie. Los datos se muestran dependiendo de si los pacientes estaban libres de arritmia (paneles de la izquierda) o de si tenían recurrencia de la arritmia (paneles de la derecha) durante el seguimiento.

En primer lugar, se puede observar que el volumen máximo (Vmax) medio tras la ACVP disminuyó en ambos, tanto en el grupo I como en el grupo II; además, no se observaron diferencias significativas en el porcentaje medio de reducción del Vmax entre los dos grupos (13 ± 12% vs 17 ± 14%, respectivamente, p = 0.217). En segundo lugar, el volumen mínimo (Vmin) medio sólo disminuyó significativamente en el grupo I. Consecuentemente, no hubo cambios significativos en la FE AI media tras la ablación en el grupo I. De hecho, la FE AI permaneció estable o aumentó en el 68% de pacientes sin recurrencia de la arritmia tras la ACVP (Figura 17), mientras que en el grupo II se observó una disminución de la FE AI media.

A 10 pacientes se les tuvo que practicar una segunda ablación, por recidiva de la FA (en 3 pacientes), o por flutter de nuevo debut (en 7 pacientes). Los cambios en la función contráctil de estos pacientes se evaluaron en la RM obtenida después del último procedimiento, correlacionándose con los observados en el resto de casos. La FE AI no mostró cambios significativos con respecto a las mediciones basales en los pacientes libres de FA después de la segunda ablación (de 35±11% a 32±7 p=0.05), mientras que la FE AI disminuyó en el resto de pacientes que presentaron recurrencia de la arritmia a pesar de los dos procedimientos (de 28±9% a 10±2%, p=0,06).

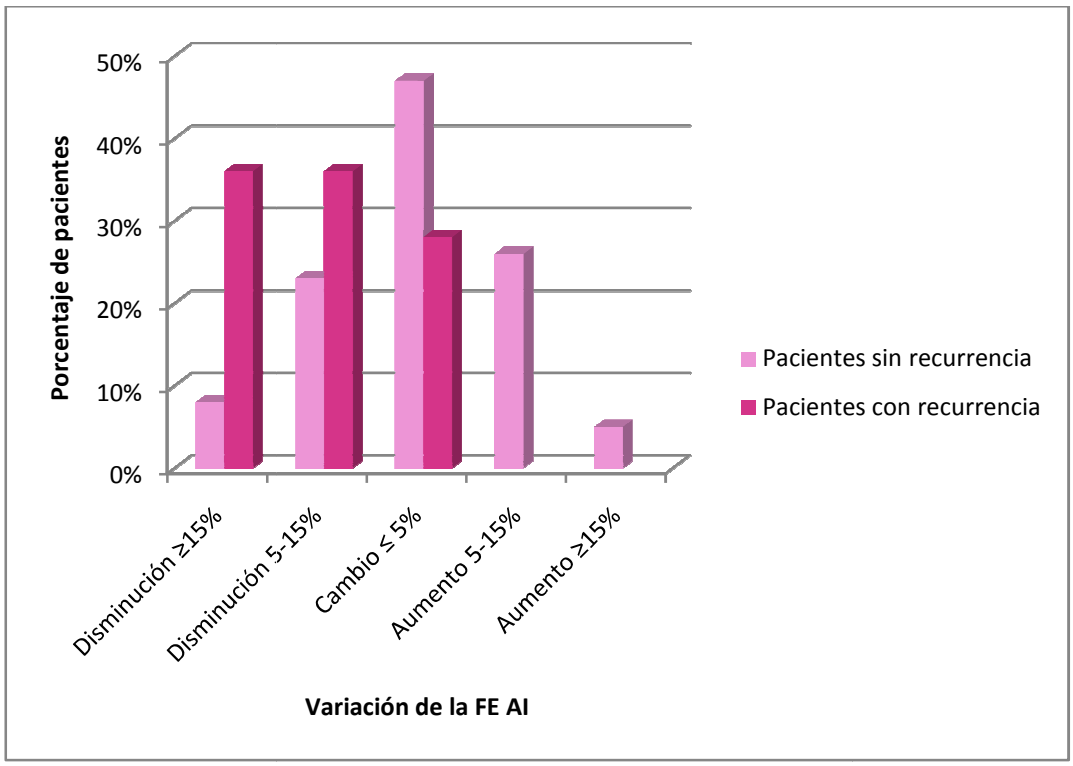

Figura 17. Variación de la fracción de eyección de la aurícula izquierda (FE AI) tras el procedimiento ablativo.

Por otra parte, la contractilidad de la OAI no mostró cambios tras la ablación. La FE de la OAI antes y después de la ACVP fue similar tanto en el grupo I (41 ± 20% vs 40 ± 20%, p = 0.8) como en el grupo II (31 ± 20% vs 32 ± 6%, p = 0.9). El grupo I presentó una reducción del volumen máximo de la OAI (de 8.8 ± 4.4 a 7.6 ± 4.4 ml, p < 0.001) y del volumen mínimo de la OAI (de 5.2 ± 4.2 a 4.3 ±3.3 ml, p <0.001) tras la ablación. En el grupo II, hubo una tendencia a la reducción del volumen máximo de la OAI (de 7.1 ± 3.4 a 6.2 ± 3.3 ml, p = 0.08), y no se observaron variaciones significativas en el volumen mínimo de la OAI (de 4.5 ± 2.1 a

4.1 ± 2.2 ml, p = 0.11) tras las ablación. La OAI presentó un comportamiento post-ablación similar al resto de la aurícula.

El análisis univariado mostró que los pacientes con recurrencias tras el procedimiento ablativo tenían mayor proporción de hipertensión arterial, volúmenes mayores de la AI (medidos antes y después de la ACVP) y menor FE AI post-ablación (Tabla 5). La única variable independiente asociada con recurrencia de la arritmia en el modelo multivariado fue el Vmin medido tras el procedimiento ablativo, con riesgo relativo de 1.04 (intervalo de confianza del 95%, 1.02-1.06, p < 0.001). El mejor valor de corte obtenido mediante el análisis de la curva ROC (receiver operating characteristic) para esta variable (área bajo la curva = 0.85) fue el Vmin ≥ 75 ml (sensibilidad = 89%, especificidad = 35%), que tenía un riesgo relativo de recurrencia de la arritmia de 11.5 (95% de intervalo de confianza, 3.8–34.5, p <0.001).

Tabla 5. Análisis univariado relacionado con el riesgo de recurrencia de la arritmia

	Riesgo relativo (95% IC)	Valor *p*
Edad (años)	1.021 (0.976-1.067)	0.366
Sexo masculine	0.986 (0.281-3.461)	0.983
FA paroxística	1.347 (0.468-3.881)	0.581
Hipertensión	3.782 (1.396-10.246)	0.009*
Cardiopatía estructural	2.078 (0.661-6.530)	0.211
Procedimientos ablativos	1.132 (0.322-3.976)	0.847
Tiempo de radiofrecuencia (min)	1.000 (0.994-1.006)	0.955
DD VI (mm)	1.036 (0.876-1.226)	0.679
DS VI (mm)	1.098 (0.908-1.328)	0.336
FE VI (%)	0.972 (0.910-1.038)	0.390
Mediciones de RM		
Vmax pre-ablación (ml)	1.026 (1.011-1.042)	0.001*
Vmin pre-ablación (ml)	1.039 (1.017-1.062)	0.001*
FE AI pre-ablación (%)	0.978 (0.936-1.021)	0.303
Vmax post-ablación (ml)	1.032 (1.009-1.056)	0.006*
Vmin post-ablación (ml)	1.044 (1.023-1.065)	<0.001*
FE AI post-ablación (%)	0.924 (0.883-0.968)	0.001*

* $p < 0.05$. IC = intervalo de confianza
DD VI = diámetro diastólico del ventrículo izquierdo; DS VI = diámetro sistólico del ventrículo izquierdo; FE VI = Fracción de eyección ventricular izquierda. (Medidas realizadas mediante ecocardiografía antes de la ablación).
RM = resonancia magnética; Vmax = volumen máximo de la auricula izquierda; Vmin = volumen mínimo de la aurícula izquierda; FE AI= fracción de eyección auricular izquierda

Left Atrial Contractility is Preserved After Successful Circumferential Pulmonary Vein Ablation in Patients with Atrial Fibrillation

ROSARIO J. PEREA, M.D., DAVID TAMBORERO, B. ENG., LLUIS MONT, M.D., PH.D., TERESA M. DE CARALT, M.D., PH.D., JOSE T. ORTIZ, M.D., ANTONIO BERRUEZO, M.D., MARIA MATIELLO, M.D., MARTA SITGES, M.D., PH.D., BARBARA VIDAL, M.D., MARCELO SANCHEZ, M.D. and JOSEP BRUGADA, M.D., PH.D.

From the Arrhythmia Section, Thorax Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain

Left Atrial Contractility. ***Introduction:*** **Circumferential pulmonary vein ablation (CPVA) for atrial fibrillation (AF) consists of creating extensive lesions in the left atrium (LA). The aim of the study was to evaluate changes in LA contractility after ablation and their relationship with procedure outcome.**

Methods and Results: **A series of 90 consecutive patients underwent cardiac magnetic resonance imaging (MRI) before and 4–6 months after CPVA. Only patients in sinus rhythm during both imaging acquisitions were included in the study to measure LA end-diastolic (LAmax) and LA end-systolic (LAmin) volumes. Fifty-five patients were finally analyzed (41 men, 52 $\pm$ 11 years, 74% paroxysmal AF). During a mean follow-up of 12 $\pm$ 7 months and after 1.2 $\pm$ 0.3 ablation procedures, 38 patients (69%) were arrhythmia-free (group I), and the remaining 17 patients had recurrences (group II). There was a significant decrease in mean LAmax volume in both groups, whereas mean LAmin volume only decreased in group I. Mean LA ejection fraction (EF) was preserved after CPVA in group I (40 $\pm$ 11% vs 38 $\pm$ 10%; $P = 0.27$) but decreased in patients with arrhythmia recurrences (37 $\pm$ 10% vs 27 $\pm$ 10%; $P < 0.001$). In fact, LA EF remained stable or increased in 68% of patients without arrhythmia recurrences.**

Conclusions: **LAmax volume reduction following CPVA occurs regardless of the clinical efficacy of the procedure, whereas mean LAmin volume only decreased in patients without recurrences. LA EF was preserved or even increased in most patients with successful CPVA.** *(J Cardiovasc Electrophysiol, Vol. 19, pp. 374-379, April 2008)*

atrial fibrillation, catheter ablation, atrial contractility

Although several studies have shown a decrease in left atrial (LA) size following atrial fibrillation (AF) ablation,[1-6] data on the response of atrial contractility are limited. A recent study in a small series found an impaired LA ejection fraction (LA EF) after paroxysmal AF catheter ablation.[7] LA EF reflects the relationship between atrial end-diastolic and end-systolic volumes, and has been proposed as a good method for evaluating global atrial contractility.[7-10] With regard to changes in LA volume after AF ablation, the data are contradictory. While some authors have reported that LA size decreases only after successful ablation,[1,3,6] others have suggested that LA size is reduced regardless of the clinical outcome of the procedure.[2,4,5] However, in the majority of these studies, LA end-diastolic (LAmax) and LA end-systolic (LAmin) volumes were not measured separately, and imaging acquisitions were performed regardless of whether the patients were in sinus rhythm or arrhythmia.

Current cardiac cine magnetic resonance imaging (MRI) techniques are accurate for depicting the anatomical structures of LA, allowing calculation of LA volumes with unusual precision.[11-15] The purpose of this study was to assess the effect of circumferential pulmonary vein ablation (CPVA) on LA volumes and LA EF, as well as their relationship with procedure outcome using cardiac MRI.

Methods

Patients

Cardiac MRI was performed before and 4–6 months after CPVA in a series of 90 consecutive patients with symptomatic, $\geq$2 drugs-refractory AF. No electrical cardioversion was performed for at least 2 weeks prior to the MRI study. A total of 55 patients were in sinus rhythm at the time of both imaging acquisitions and were included in this study. LAmax and LAmin volumes were measured and LA EF was calculated.

Paroxysmal AF was defined as AF that terminates spontaneously. Persistent AF was defined as AF lasting more than 7 days or requiring electrical cardioversion to be terminated. Patients with continuous AF in whom cardioversion had either failed or had not been attempted were classified as having permanent AF and were excluded from the study.

The study was funded in part by a grant from the Carlos III Health Institute, Madrid, Spain (*Fondo Investigación Sanitaria-PI050081*).

The first two authors have contributed equally to this study.

Address for correspondence: Dr. Lluis Mont, Arrhythmia Section, Thorax Institute, Hospital Clinic, University of Barcelona, Villarroel 170, 08036 Barcelona. Fax: 0034-93-451-3045; E-mail: lmont@clinic.ub.es

Manuscript received 13 June 2007; Revised manuscript received 26 October 2007; Accepted for publication 31 October 2007.

doi: 10.1111/j.1540-8167.2007.01086.x

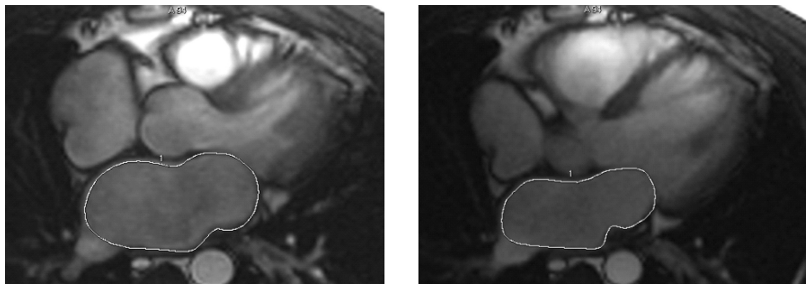

Figure 1. *In a gradient-echo sequence the boundaries of the left atrium at maximum dilation (left panel) and at maximum contraction (right panel) are manually drawn for each slice. Left atrial maximal and minimal volumes were both calculated by the disc-summation technique (Simpson's rule).*

The study population was divided into two groups: those arrhythmia-free after the ablation procedure (group I) and those with recurrences during follow-up (group II) beyond a one-month blanking period (see follow-up section). Patients were included after written informed consent was obtained. The protocol study was approved by the hospital's Ethics Committee.

Magnetic Resonance Imaging

Image acquisition

Cardiac MRI was performed using a 1.5 Tesla scanner (Signa Horizon CV, GE Medical Systems, Milwaukee WI, USA) using a dedicated cardiac phase-array coil. Image acquisition was gated by surface electrocardiogram during breath-hold at end-exhalation. Fast spoiled gradient-echo localizer scans were performed in sagittal and axial views. A segmented gradient-echo cine sequence (FIESTA) was then carried out in the axial plane to cover the entire heart. Sequence parameters were as follows: TE 1.6 ms, TR 3.7 ms, 45° flip angle, matrix size 256 × 256, field of view 360–440 mm, slice thickness 10 mm without gap, and 125 kHz receiver bandwidth. The time of acquisition varied according to the heart rate. A 3D magnetic resonance angiography in the axial plane was acquired following intravenous administration of a gadolinium-based contrast bolus at a dose of 0.75 mg/kg. The 3D angiographic and volume rendered data sets were registered with the electroanatomic maps to locate the pulmonary veins (PVs) and their connections to the LA and to assist with the ablation procedure.

Image analysis

LAmax volume was measured on the frame before mitral valve opening was identified and the LAmin volume was quantified on the first frame showing mitral valve closure. The inner contours of the LA were manually traced for all sequential axial cine images with digital markers excluding the PVs at their ostia and the LA appendage (LAA) (Fig. 1). The actual atrial volumes were calculated by disc summation (Simpson's rule). LA EF was then calculated as follows: (LAmax − LAmin/LAmax) ×100. Additionally, the contractility of the LAA was evaluated by calculating the LAA EF. For this purpose, LAA diastolic and systolic volumes were measured independently from the atrial region.

All data sets were analyzed by two independent radiologists blinded to clinical outcomes. A maximal discordance of 5% in the volume estimation was accepted. When a higher discordance was observed, measurements were repeated. Final measurements were recorded as the average of the two observations for all parameters.

Ablation Procedure

Conventional transthoracic echocardiography plus transesophageal echocardiography were performed prior to the ablation procedure in order to discard intracavitary thrombus. Continuous radiofrequency lesions were delivered after transseptal access as described elsewhere[16-18] surrounding each ipsilateral PV. Ablation lines were also deployed along LA roof, LA posterior wall, and mitral isthmus by a thermocouple-equipped 3.5 mm cooled tip catheter at a target temperature of 50°C and a maximum output from 35 to 40 W (Fig. 2). The endpoint of the ablation procedure was to reduce the amplitude of the local electrogram inside the surrounded area to below 0.15 mV. Ablation lines were created anatomically with the aid of a three-dimensional LA reconstruction performed by the CARTO (Biosense Webster) or NaVx (Endocardial Solutions) navigation systems. After circumferential lines were completed, the assessment of the electrogram abatement was performed in sinus rhythm (after cardioversion if needed) at several sites within the encircled antrum and inside each PV by the ablation catheter itself.

Follow-up

Patients were followed up as outpatients at 1, 4, and 7 months following the ablation procedure, and every six months thereafter if they remained asymptomatic. Routine 24- or 48-hour Holter monitoring was performed before each visit and patients were also asked to communicate any symptom suggestive of AF recurrence between scheduled visits.

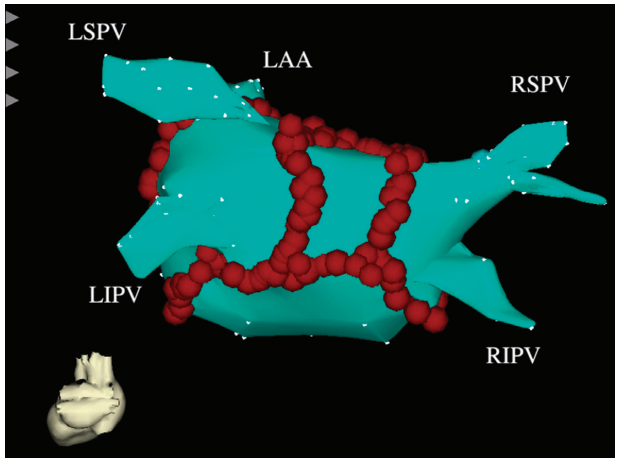

Figure 2. *Three-dimensional anatomical reconstruction of the left atrium (posteroanterior view) showing ablation scheme. Red dots represent radiofrequency delivery sites. LAA = left atrial appendage; PV = pulmonary vein; LSPV = left superior PV; LIPV = left inferior PV; RSPV = right superior PV; RIPV = right inferior PV.*

TABLE 1
Patient Characteristics

Age (years)	52.0 ± 11.3
Male gender	44 (80.0%)
Type of AF	
Paroxysmal	41 (74.5%)
Persistent	14 (25.5%)
Hypertension	12 (21.8%)
Structural heart disease	9 (16.3%)
LV DD (mm)	52.4 ± 4.7
LV SD (mm)	33.1 ± 3.8
LV EF (%)	60.0 ± 8.8
AF evolution time (years)	8.4 ± 8.1

All patients continued oral anticoagulation to maintain an international normalized ratio between 2.0 and 3.0 for a minimum of 2 months after ablation. All patients received antiarrhythmic drugs (flecainide in the absence of structural heart disease or amiodarone otherwise) at least during the first 4 weeks after the procedure in order to manage early recurrences. CPVA was considered successful if no arrhythmias were recorded during the follow-up after a 5-week blanking period without antiarrhythmic treatment or with the use of one previously ineffective drug. Minimum follow-up of this series was 6 months.

Statistical Analysis

Quantitative data are reported as mean ± SD. MRI measures before and after ablation between subjects were compared using a paired Student's *t*-test. The relationship between patient variables and the time to recurrence during follow-up was evaluated using survival analysis methodology (Cox regression models). Variables were included in the multivariate analysis using a forward stepwise procedure with criteria of $P < 0.05$ for inclusion and $P > 0.10$ for removal from the model. A two-sided P-value ≤ 0.05 was considered statistically significant. The analyses were performed using the SPSS 12.0 statistical package (SPSS, Chicago, IL, USA).

Results

From a series of 90 consecutive patients, 35 were excluded because they were not in sinus rhythm at the time of the first and/or second MRI studies. Therefore, a total of 55 patients were finally analyzed. Their baseline characteristics are summarized in Table 1.

Thirty-eight patients (69.1%) were arrhythmia-free (group I), whereas the remaining 17 patients had arrhythmia recurrences (group II) after 1.2 ± 0.3 ablation procedures and a mean follow up of 11.8 ± 7.2 months (15 patients with AF relapses and two patients with new-onset LA flutter). Among patients with successful ablation, 33 (60%) were without antiarrhythmic drug treatment, three patients received flecainide to manage symptomatic premature atrial contractions, and two patients were arrhythmia-free under either flecainide or amiodarone treatment that started during blanking period and was not stopped afterwards by the referring physician.

Table 2 shows the changes in LA measurements after CPVA according to procedure outcome. Figure 3 shows the same data for each patient in the series. Firstly, it can be observed that mean LAmax volume after CPVA decreased in both group I and group II; furthermore, no differences in the mean percentage of LAmax volume reduction were observed between the two groups (13 ± 12% vs 17 ± 14%, respectively, $P = 0.217$). Secondly, mean LAmin volume only decreased significantly in group I. Consequently, there were no significant changes in the mean LA EF after ablation in group I, whereas a decrease in the mean LA EF was seen in group II. In fact, LA EF remained stable or increased in 68% of patients without arrhythmia recurrences after CPVA (Fig. 4).

On the other hand, the contractility of the LAA showed no change after ablation. EF of the LAA before and after CPVA was similar in both group I (41 ± 20% vs 40 ± 20%, $P = 0.8$) and group II (31 ± 20% vs 32 ± 6%, $P = 0.9$). In group I, there was a reduction in LAA diastolic volume (from 8.8 ± 4.4 to 7.6 ± 4.4 mL, $P < 0.001$) and in LAA systolic volume (from 5.2 ± 4.2 to 4.3 ± 3.3 mL, $P < 0.001$) after ablation. In group II, there was a trend to LAA diastolic volume reduction (from 7.1 ± 3.4 to 6.2 ± 3.3 mL, $P = 0.08$), and no significant changes in LAA systolic volume (from 4.5 ± 2.1 to 4.1 ± 2.2 mL, $P = 0.11$) after ablation.

Univariate analysis showed that patients with recurrences after the ablation procedure had a higher proportion of hypertension, larger LA volumes (measured before and after CPVA) and lower postablation LA EF (Table 3). The only variable independently associated with arrhythmia recurrence in the multivariate model was the LAmin volume measured after the ablation procedure, with a hazard ratio of 1.04 (95% confidence interval, 1.02–1.06, $P < 0.001$). The best cut-off obtained by receiver operating characteristic (ROC) analysis for this variable (area under curve = 0.85) was LAmin volume ≥75 mL (sensitivity = 89%, specificity = 35%), which had a hazard ratio for arrhythmia recurrence of 11.5 (95% confidence interval, 3.8–34.5, $P < 0.001$).

Discussion

The main finding of this study is that LA contractility evaluated by means of LA EF is preserved or even increased

TABLE 2
Left Atrial Values Before and 4–6 Months After Ablation Procedure

	No Recurrences (n = 38)				Recurrences (n = 17)			
	Pre CPVA	**Post CPVA**	**Mean Decrease**	**P-Value**	**Pre CPVA**	**Post CPVA**	**Mean Decrease**	**P-Value**
LAmax (mL)	98.0 ± 19.9	84.9 ± 17.1	13%	<0.001*	126.2 ± 32.8	103.5 ± 28.1	17%	<0.001*
LAmin (mL)	58.6 ± 16.1	52.2 ± 12.1	10%	0.004*	78.4 ± 22.2	75.8 ± 24.3	4%	0.315
LA EF (%)	40.2 ± 11.5	38.1 ± 9.8	2%	0.268	37.4 ± 10.1	26.9 ± 10.2	11%	<0.001*

*Means P< 0.05.
LAmax = left atrial maximal volume; LAmin = left atrial minimal volume; LAEF = left atrial ejection fraction; pre/post CPVA = previous/posterior to circumferential pulmonary vein ablation.

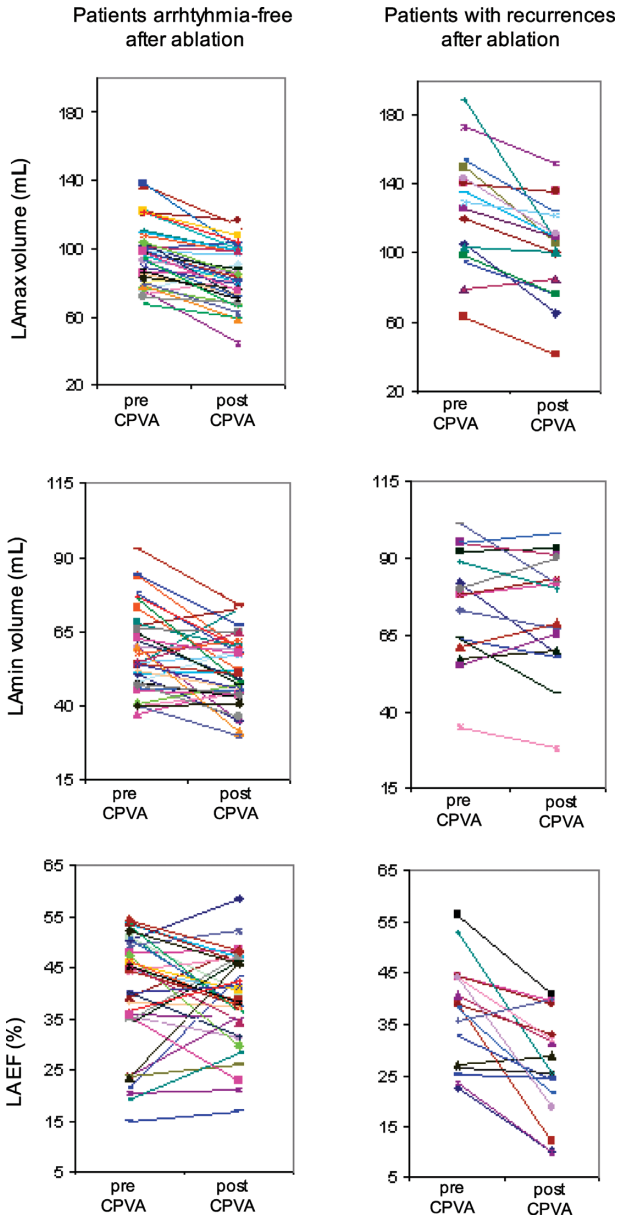

Figure 3. *Evolution of left atrial (LA) end-diastolic (LAmax) volume, LA end-systolic (LAmin) volume and LA ejection fraction (LA EF) 4-6 months after circumferential pulmonary vein ablation (CPVA) in each patient in the series. Data are shown depending on whether patients were arrhythmia-free (left panels) or had arrhythmia recurrences (right panels) during the follow-up.*

after CPVA in the majority of patients who had no arrhythmia recurrences after ablation. In fact, our data showed a similar reduction of LAmax volume in all patients, regardless of the ablation outcome, whereas mean LAmin volume only decreased in those showing a successful outcome of the procedure. Previous data regarding this issue have proven contradictory. Some investigators have reported that LA size after AF ablation decreased significantly only after a successful procedure, whereas LA size remained unchanged or even increased in the remaining patients.[1,3,6] In contrast, other investigators have found that LA size after AF ablation decreased in all patients regardless of the procedure outcome.[2,4,5]

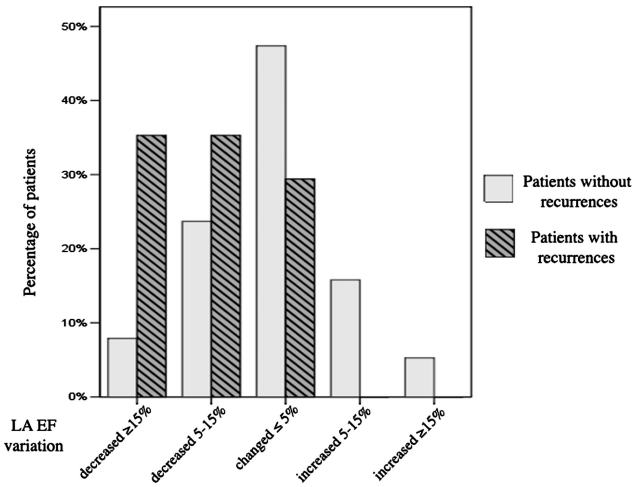

Figure 4. *Variation of left atrial ejection fraction (LA EF) following ablation procedure.*

There could be several reasons for these discrepancies. First, different image techniques were used: echocardiography,[1,4-6] magnetic resonance angiography,[2] or computed tomography.[3] Second, LA size was determined using different measures: LA anteroposterior diameter,[4,6] LA three orthogonal diameters,[1,2,5] or LA volume.[3] Third, with the exception of one reported study,[6] only the maximal atrial dimension was measured. Last, in the majority of these studies, the LA measurements did not take into account whether patients were in AF or not at the time of image acquisition.[2-4,6] This could interfere with a correct measurement of the LA volume variation after ablation. In fact, if one of the LA images was acquired during AF and the other in sinus rhythm, it may overestimate the variation of LAmin. In the present study, in order to calculate LA EF, LAmax, and LAmin volumes were determined separately. Therefore, only patients who were in

TABLE 3
Univariate Analysis Related to the Risk of Arrhythmia Recurrence

	Hazard Ratio (95% CI)	P-Value
Age (years)	1.021 (0.976–1.067)	0.366
Male gender	0.986 (0.281–3.461)	0.983
Paroxysmal AF	1.347 (0.468–3.881)	0.581
Hypertension	3.782 (1.396–10.246)	0.009*
Structural heart disease	2.078 (0.661–6.530)	0.211
Ablation procedures	1.132 (0.322–3.976)	0.847
Radiofrequency time (min)	1.000 (0.994–1.006)	0.955
LV DD (mm)	1.036 (0.876–1.226)	0.679
LV SD (mm)	1.098 (0.908–1.328)	0.336
LV EF (%)	0.972 (0.910–1.038)	0.390
MRI measurements		
Preablation LAmax (mL)	1.026 (1.011–1.042)	0.001*
Preablation LAmin (mL)	1.039 (1.017–1.062)	0.001*
Preablation LA EF (%)	0.978 (0.936–1.021)	0.303
Postablation LAmax (mL)	1.032 (1.009–1.056)	0.006*
Postablation LAmin (mL)	1.044 (1.023–1.065)	<0.001*
Postablation LA EF (%)	0.924 (0.883–0.968)	0.001*

* $P < 0.05$.
LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter; LV EF = left ventricular ejection fraction. (Measurements performed by echocardiography prior to ablation.)
MRI = magnetic resonance imaging; LAmax = left atrial maximal volume; LAmin = left atrial minimal volume; LA EF = left atrial ejection fraction.

sinus rhythm at both assessments were included to ensure optimal measurements, and no electrical cardioversion was performed during the 2 weeks preceding the MRI in order to avoid "stunning" of the atrial mechanical function.[19] Furthermore, cardiac-gated cine MRI and the disc-summation technique (Simpson's rule) were used to measure both LA volumes to avoid geometric assumptions, image plane positioning errors, and inappropriate sampling of the atrial boundaries.[20–22] It is conceivable that all these methodological limitations could explain the observed discrepancies in the literature.

To our knowledge, two recent studies have analyzed LA EF after AF ablation, showing contradictory data.[7,23] Verma *et al*. reported a improvement in atrial function in a series of 67 patients evaluated by either echocardiography or cine electron beam CT, whereas Lemola *et al*. suggested a deterioration of atrial contractility in a series of 10 paroxysmal AF patients evaluated by 3D CT. However, the authors compared contractility regardless of the success of the procedure. According to our data, LA EF after ablation generally worsened in patients with recurrences. In fact, whereas LAmax volume reduction occurred in almost all patients, mean LAmin volume only decreased in patients without recurrences. Moreover, LAmin volume after CPVA was the only independent variable related to procedure success in the multivariate analysis. Most patients with a successful ablation showed a decrease in both LAmax and LAmin volumes and preserved contractility. Whether the LAmin volume reduction in these cases occurred immediately after ablation due to tissue shrinking as a result of the radiofrequency delivery,[24] or if it was subsequent to a mid-term reverse remodeling secondary to the maintenance of stable sinus rhythm,[25] remains inconclusive in the present study. Another hypothesis that may be taken into account is that the PVs isolation may lead to loss of their contractile capability, and this could cause blood regurgitation from the LA through the PVs during atrial systole. This fact might result in a decrease in atrial systolic volume and an improvement in LA ejection fraction. More data are required to elucidate whether the LAmin decrease was a cause or a consequence of the outcome of the procedure.

Finally, LAA contractility was not compromised after CPVA in any patient of this series. Changes in LAA volumes were in accordance with those observed in the whole LA, although to a lesser extent. This could be due to the fact that RF energy is deployed out of the LAA and the effect of tissue shrinkage may be lower. However, there are methodological limitations in the measurement of volumes in such a small structure. As a consequence, a broader population would be needed to study these subtle differences on detail.

Study Limitations

The impossibility of accurately measuring the AF burden at each time point[25] could partly affect the evaluation of LA contractility. This is a limitation in this type of study, since asymptomatic AF episodes could be misinterpreted unless continuous monitoring of the patient was performed.

In the present study, certain details of the imaging technique should be noted. First, image acquisition was carried out at end-exhalation. Imaging during inspiration may have produced different results related to changes in diastolic relaxation properties and preload conditions. Second, end-systole and end-diastole were defined using direct visualization of mitral valve opening and closure, since electrocardiogram co-registration is not available for MRI image post processing. Finally, PV ostium was defined at the point of inflection between PV and LA wall. This simplification was used to facilitate identification and promote interobserver reproducibility. However, these limitations are unlikely to have had a significant effect on the results of the study since both basal and follow-up measurements were performed in the same manner, and LA variations between subjects may reflect real changes.

On the other hand, the effect of radiofrequency may be more significant in those patients who underwent two ablations, since changes in LA contractility were evaluated in the MRI obtained after the second procedure. However, results in these 10 patients were consistent with those observed in the remaining cases. In fact, LA EF showed no significant changes with respect to the basal measurement in arrhythmia-free patients after the second ablation (from $35 \pm 11\%$ to $32 \pm 7\%$, $P = 0.50$), whereas LA EF decreased considerably in the remaining patients suffering arrhythmia recurrences in spite of the two procedures (from $28 \pm 9\%$ to $10 \pm 2\%$, $P = 0.06$). Furthermore, in seven of the 10 second procedures, the amount of radiofrequency delivery was low because only new-onset LA flutter was ablated and no extensive lesions were created.

Finally, it should be considered that the results of this study may vary depending on the ablation approach. However, the effect on LA contractility is unlikely to be greater in other ablation procedures, taking into account the extensive lesions created in CPVA.

Conclusions

LAmax volume reduction after CPVA occurs regardless of the clinical efficacy of the procedure, whereas LAmin volume decreased only in patients free of arrhythmia recurrences. LA EF was preserved or even increased in the majority of patients after successful CPVA.

References

1. Beukema WP, Elvan A, Sie HT, Misier AR, Wellens HJ: Successful radiofrequency ablation in patients with previous atrial fibrillation results in a significant decrease in left atrial size. Circulation 2005;112:2089-2095.
2. Jayam VK, Dong J, Vasamreddy CR, Lickfett L, Kato R, Dickfeld T, Eldadah Z, Dalal D, Blumke DA, Berger R, Halperin HR, Calkins H: Atrial volume reduction following catheter ablation of atrial fibrillation and relation to reduction in pulmonary vein size: An evaluation using magnetic resonance angiography. J Interv Card Electrophysiol 2005;13:107-114.
3. Lemola K, Sneider M, Desjardins B, Case I, Chugh A, Hall B, Cheung P, Good E, Han J, Tamirisa K, Bogun F, Pelosi F Jr, Kazerooni E, Morady F, Oral H: Effects of left atrial ablation of atrial fibrillation on size of the left atrium and pulmonary veins. Heart Rhythm 2004;1:576-581.
4. 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.
5. Reant P, Lafitte S, Jais P, Serri K, Weerasooriya R, Hocini M, Pillois X, Clementy J, Haissaguerre M, Roudaut R: Reverse remodeling of the left cardiac chambers after catheter ablation after 1 year in a series of patients with isolated atrial fibrillation. Circulation 2005;112:2896-2903.

6. Tops LF, Bax JJ, Zeppenfeld K, Jongbloed MR, Van Der Wall EE, Schalij MJ: Effect of radiofrequency catheter ablation for atrial fibrillation on left atrial cavity size. Am J Cardiol 2006;97:1220-1222.
7. Lemola K, Desjardins B, Sneider M, Case I, Chugh A, Good E, Han J, Tamirisa K, Tsemo A, Reich S, Tschopp D, Igic P, Elmouchi D, Bogun F, Pelosi F, Kazerooni E, Morady F, Oral H: Effect of left atrial circumferential ablation for atrial fibrilation on left atrial transport function. Heart Rhythm 2005;2:923-928.
8. Yamanaka K, Fujita M, Doi K, Tsuneyoshi H, Yamazato A, Ueno K, Zen E, Komeda M: Multislice computed tomography accurately quantifies left atrial size and function after the MAZE procedure. Circulation 2006;114:I5-I9.
9. Gentlesk PJ, Sauer WH, Gerstenfeld EP, Lin D, Dixit S, Zado E, Callans PCD, Marchlinski FE: Reversal of left ventricular dysfunction following ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2007;18:9-14.
10. Thomas L, Boyd A, Thomas SP, Schiller NB, Ross DL: Atrial structural remodelling and restoration of atrial contraction after linear ablation for atrial fibrillation. Eur Heart J 2003;24:1942-1951.
11. 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.
12. Mogelvang J, Lindvig K, Sondergaard L, Saunamaki K, Henriksen O: Reproducibility of cardiac volume measurements including left ventricular mass determined by MRI. Clin Physiol 1993;13:587-597.
13. Pattynama PM, Lamb HJ, Van Der Velde EA, Van Der Wall EE, de Roos A: Left ventricular measurements with cine and spin-echo MR imaging: A study of reproducibility with variance component analysis. Radiology 1993;187:261-268.
14. Shapiro EP, Rogers WJ, Beyar R, Soulen RL, Zerhouni EA, Lima JA, Weiss JL: Determination of left ventricular mass by magnetic resonance imaging in hearts deformed by acute infarction. Circulation 1989;79:706-711.
15. Mohiaddin RH, Hasegawa M: Measurement of atrial volumes by magnetic-resonance-imaging in healthy-volunteers and in patients with myocardial-infarction. Eur Heart J 1995;16:106-111.
16. 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.
17. 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.
18. Berruezo A, Tamborero D, Vidal B, Sitges M, Matiello M, Molina I, Mont LL, Brugada J: Preprocedural predictors of recurrences after electroanatomical encircling of pulmonary veins. Eur Heart J 2006;27:869-870.
19. Thomas MD, Kalra PR, Jones A, Struthers AD, More RS: Time course for recovery of atrial mechanical and endocrine function post DC cardioversion for persistent atrial fibrillation. Int J Cardiol 2005;102:487-491.
20. Jarvinen V, Kupari M, Hekali P, Poutanen VP: Assessment of left atrial volumes and phasic function using cine magnetic resonance imaging in normal subjects. Am J Cardiol 1994;73:1135-1138.
21. Jarvinen VM, Kupari MM, Hekali PE, Poutanen VP: Right atrial MR imaging studies of cadaveric atrial casts and comparison with right and left atrial volumes and function in healthy subjects. Radiology 1994;191:137-142.
22. Keller AM, Gopal AS, King DL: Left and right atrial volume by freehand three-dimensional echocardiography: In vivo validation using magnetic resonance imaging. Eur J Echocardiogr 2000;1:55-65.
23. Verma A, Kilicaslan F, Adams JR, Hao S, Beheiry S, Minor S, Ozduran V, Elayi SC, Martin DO, Schweikert RA, Saliba W, Thomas JD, Garcia M, Klein A, Natale A: Extensive ablation during pulmonary vein antrum isolation has no adverse impact on left atrial function: An echocardiography and cine computed tomography analysis. J Cardiovasc Electrophysiol 2006;17:741-746.
24. Victal OA, Teerlink JR, Gaxiola E, Wallace AW, Najar S, Camacho DH, Gutierrez A, Herrera G, Zuniga G, Mercado-Rios F, Ratcliffe MB: Left ventricular volume reduction by radiofrequency heating of chronic myocardial infarction in patients with congestive heart failure. Circulation 2002;105:1317-1322.
25. Zipes DP: Atrial fibrillation. A tachycardia-induced atrial cardiomyopathy. Circulation 1997;95:562-564.

ESTUDIO 2

Incidence of pulmonary vein stenosis in patients submitted to atrial fibrillation ablation: a comparison of the selective segmental ostial ablation vs the circumferential pulmonary veins ablation.

Tamborero D, Mont L, Nava S, Caralt TM, Molina I, Scalise A, **Perea RJ**, Bartholomay E, Berruezo A, Matiello M, Brugada J.

***J Interv Card Electrophysiol*.** 2005;14:21-25.

3.2.1 OBJETIVOS

Objetivo general

El objetivo general de este estudio es demostrar la capacidad de la RM para el estudio anatómico sistemático de las VPs y de la AI en pacientes tributarios de APRF de las VPs.

Objetivo específico

Identificar la aparición de estenosis de las VPs como complicación del procedimiento en el estudio post-ablación y determinar su relación con la técnica ablativa empleada.

3.2.2 RESULTADOS

Se realizó ARM en 73 de 78 pacientes consecutivos sometidos a APRF de la FA. La ARM no se pudo realizar en 3 pacientes con claustrofobia, en un paciente con marcapasos y en otro con desfibrilador automático implantable. Las características demográficas de los pacientes de encuentran resumidas en la Tabla 6. La ablación se realizó mediante el procedimiento de ASOS en 32 pacientes; en 41 pacientes la ablación se realizó mediante el método de ACVP. Durante un período medio de seguimiento de 14.7 ± 12.2 meses, 23 y 31 pacientes de los grupos de ASOS y de ACVP se mantuvieron libres de recurrencias (72% vs 76% libres de arritmias, long rank test p = NS).

Tabla 6. Características demográficas

	Grupo ASOS	Grupo ACVP	P
Pacientes	32	41	
FA paroxística	27 (85%)	27 (66%)	0.09
Duración de la FA (meses)	62 ± 71	72 ± 80	NS
Número de FAA fallidos	2.5 ± 0.9	2.6 ± 0.7	NS
Edad (años)	50 ± 12	52 ± 10	NS
Sexo masculino	23 (75%)	33 (80%)	NS
Aurícula izquierda (mm)	37 ± 4	42 ± 5	0.02
FEVI (%)	58 ± 11	53 ±17	NS
Cardiopatía estructural	8 (25%)	11 (27%)	NS
Hipertensión arterial	9 (28%)	12 (29%)	NS

ASOS: Ablación segmentaria ostial selectiva. ACVP: Ablación circunferencial de las venas pulmonares. FAA: Fármacos antiarrítmicos. FEVI: Fracción de eyección ventricular izquierda.

Ninguno de los pacientes desarrolló síntomas sugestivos de estenosis de las VPs. Sin embargo, en 6 pacientes se detectó estenosis significativa de las VPs en una ARM de rutina, todas ellas en el grupo de ASOS, ninguna en el grupo de ACVP (18.8% vs 0% de los pacientes

evaluados; p = 0.005). En 4 pacientes, la estenosis se localizó en la VPSI, en 1 paciente en la VPII y en 1 paciente tanto la VPSI como la VPII tenían estenosis significativa.

En el grupo de ACVP, las líneas de ablación rodeaban todas las VPs en todos los casos. En el grupo de ASOS se trató una media de 1.8 ± 0.7 VPs por paciente con una media de 10.3 ± 0.8 minutos de aplicación de radiofrecuencia. Los segmentos ostiales donde se aplicó la radiofrecuencia para conseguir la desconexión eléctrica de la VP fueron clasificados, mediante una guía anatómica y fluoroscópica, en 4 divisiones ostiales: segmento anterior, posterior, superior e inferior. En nuestra serie, la actividad eléctrica más precoz se registró en el segmento inferior en el 57 y 58% de las VPSIs y VPSDs tratadas, respectivamente (Tabla 7). La VPSI se aisló en el 93.8% de pacientes, la VPII en el 18.8%, la VPSD en el 59.4% y la VPID en el 6.3%. Fue necesario un segundo procedimiento en 3 pacientes del grupo de ASOS debido a recurrencia de la FA, por tanto el número total de VPs aisladas fue de 33 VPSIs, 6 VPIIs, 21 VPSDs y 2 VPIDs. En conjunto, un 15.2% de las VPSIs y un 33.3% de las VPIIs tratadas con ASOS desarrollaron estenosis (Figura 18).

Tabla 7. Segmentos del *ostium* de las VPs en que se aplicó la energía de radiofrecuencia en el grupo de ASOS

	Inferior (%)	Posterior (%)	Superior (%)	Anterior (%)
VPSI (*n* = 30)	56.6	26.6	23.3	26.6
VPSD (*n* = 19)	57.9	26.3	21.0	21.0
VPII (*n* = 6)	16.7	33.3	50.0	16.7
VPID (*n* =2)	0	0	100	100

VPs: venas pulmonares. ASOS: ablación segmentaria ostial selectiva. VPSI: vena pulmonar superior izquierda. VPSD: vena pulmonar superior derecha. VPII: vena pulmonar inferior izquierda. VPID: vena pulmonar inferior derecha.

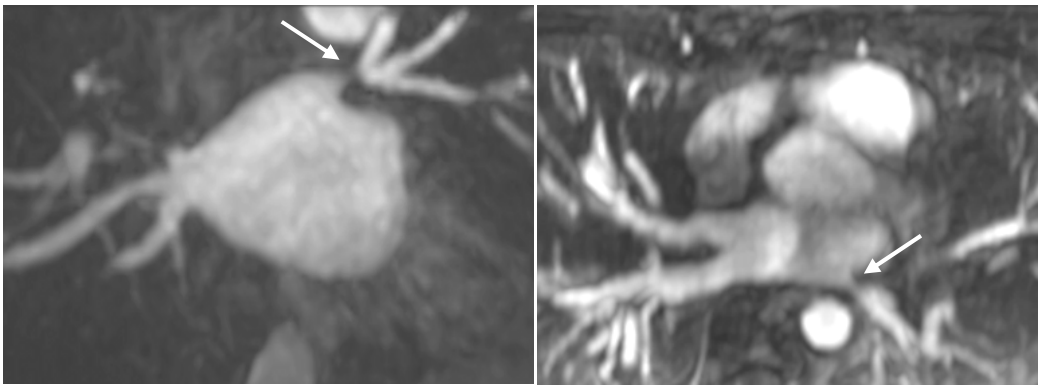

Figura 18. Angio-resonancia magnética. Reconstrucción tridimensional de la aurícula izquierda y de las venas pulmonares; a) proyección oblicua anteroposterior que muestra estenosis post-ablación de la vena pulmonar superior izquierda (flecha); y b) proyección oblicua superoinferior que muestra estenosis de la vena pulmonar inferior izquierda (flecha).

No se encontraron diferencias en las características de los pacientes o en los detalles del procedimiento entre los pacientes con y sin estenosis en el grupo de ASOS, y no se pudieron identificar predictores de estenosis.

En nuestra serie, 16 pacientes (22% del total) tuvo alguna variante anatómica de las VPs, siendo la más frecuente la presencia de un tronco común izquierdo (15% de los pacientes) y la presencia de una VPMD (5% de los pacientes) (Figura 19).

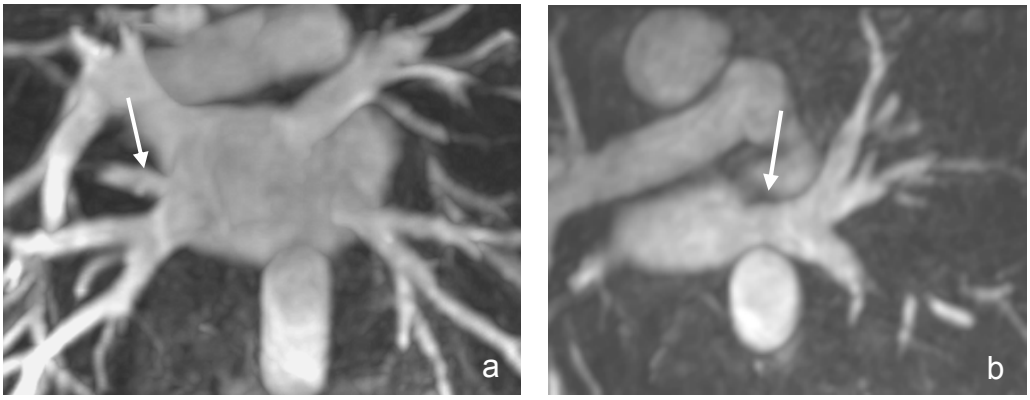

Figura 19. Angio-resonancia magnética. Reconstrucciones multiplanares que muestran variantes anatómicas de las venas pulmonares; a) Vena pulmonar media derecha (flecha); b) tronco común izquierdo (flecha).

Journal of Interventional Cardiac Electrophysiology 14, 21–25, 2005

Incidence of Pulmonary Vein Stenosis in Patients Submitted to Atrial Fibrillation Ablation: A Comparison of the Selective Segmental Ostial Ablation vs the Circumferential Pulmonary Veins Ablation

David Tamborero, Lluis Mont, Santiago Nava, Teresa M. de Caralt, Irma Molina, Andrea Scalise, Rosario J. Perea, Eduardo Bartholomay, Antonio Berruezo, Maria Matiello, and Josep Brugada

Cardiovascular Institute, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic, University of Barcelona

Abstract. ***Introduction:*** **Pulmonary vein (PV) stenosis is an important complication of the AF ablation and could be underestimated if their assessment is not systematically done. Selective Segmental Ostial Ablation (SSOA) and Circunferential Pulmonary Veins Ablation (CPVA) have demonstrated efficacy in atrial fibrillation (AF) treatment. In this study the real incidence of PV stenosis in patients (pts) submitted to both SSOA and CPVA was compared.**

Methods: **Those pts with focal activity and normal left atrial size were submitted to SSOA, remaining pts were submitted to CPVA to treat refractory, symptomatic AF. Contrast enhanced magnetic resonance angiography (MRA) was routinely performed in all patients 4 months after the procedure.**

Results: **A series of 73 consecutive patients (mean age of 51 ± 11 years; 75% male) were included. SSOA was performed in 32 patients, and the remaining 41 patients underwent to CPVA, obtaining similar efficacy rates (72% vs 76% arrythmia free probability at 12 months; log rank test p = NS). Six patients had a significant PV stenosis, all in SSOA group none in CPVA group (18.8% vs 0%; $p = 0.005$). All patients were asymptomatic and the stenosis was detected in routine MRA. No predictors of stenosis has been identified analysing patient procedure characteristics.**

Conclusion: **PV stenosis is a potential complication of SSOA not seen in CPVA. The study confirms than MRA is useful for identifying patients with asymptomatic PV stenosis.**

Key Words. **atrial fibrillation, pulmonary veins stenosis, catheter ablation**

Introduction

Pulmonary vein (PV) radiofrequency (RF) ablation is a curative procedure for patients with atrial fibrillation (AF). Several strategies have been developed to achieve the PV isolation with good clinical results [1–3]. PV stenosis has been recognized as one potential complication of the ablation procedure that can be associated with severe respiratory symptoms that cause significant morbidity [4–7]. Its incidence is unclear, mainly in asymptomatic patients. Several methods have been evaluated for the proper detection of this complication [8] and Magnetic Resonance Angiography (MRA) has become a useful method for the diagnosis [9,10].

The aim of this study was to analyse the incidence of PV stenosis in patients treated with selective segmental ostial ablation (SSOA) or with circumferential pulmonary veins ablation (CPVA) methods.

Methods

Patients

A series of 73 consecutive patients underwent to AF ablation for treatment of drug-refractory, symptomatic AF. All patients were previously studied with 24-hours Holter monitoring and

Santiago Nava, A. Berruezo and A. Scalise were supported in part by a Grant from the Fundació Clínic per la Recerca Biomèdica.

Address for correspondence: Lluís Mont, MD, PhD, Cardiovascular Institute, Hospital Clínic Universitari de Barcelona, Villarroel 170, Barcelona 08036, Catalonia, Spain. E-mail: lmont@clinic.ub.es

Received 25 July 2005; accepted 22 August 2005

Table 1. *Demographic characteristics*

	SSOA group	CPVA group	P
Patients	32	41	
Paroxysmal AF	27 (85%)	27 (66%)	0.09
Duration of AF (months)	62 ± 71	72 ± 80	NS
Number of failed AAD	2.5 ± 0.9	2.6 ± 0.7	NS
Age (years)	50 ± 12	52 ± 10	NS
Male Sex	23 (75%)	33 (80%)	NS
Left Atrium (mm)	37 ± 4	42 ± 5	0.02
LVEF (%)	58 ± 11	53 ± 17	NS
Structural Heart Disease	8 (25%)	11 (27%)	NS
Arterial Hypertension	9 (28%)	12 (29%)	NS

SSOA: Selective Segmental ostial ablation. CPVA: Circumferential pulmonary veins ablation. AAD: Antiarrhythmic drugs. LVEF: Left ventricular ejection fraction.

transthoracic echocardiography. Informed consent was obtained in all patients before the procedure. Patients with suspected focal origin AF (identified by structurally normal left atria and >10 runs of atrial tachycardia/24 hours) were submitted to SSOA in order to isolate pulmonary veins (PV) from left atria. The remaining patients underwent to CPVA to modify atrial substrate with extended lesions. Demographic characteristics are presented in Table 1.

Ablation Procedure

Selective Segmental Ostial Ablation. After transseptal access, PV disconnection was performed as described by Haissaguerre et al. [1]. A decapolar Lasso catheter (Biosense-Webster) was used to map the PV potentials and RF energy was applied by a thermocouple-equipped 4 mm tip catheter (Biosense-Webster). Ostial lesions were created where the PV earliest activity was recorded until PV potentials were eliminated or dissociated at a target temperature of 50°C and a maximum output from 40 to 50 W. Only those PVs with electrical activity were treated. No attempts to induce premature beats were done. Details of the approach used have been previously reported [13].

Circumferential Pulmonary Veins Ablation. Non-fluoroscopic navigation system (CARTO; Biosense Webster) was used to delineate the left atria and PVs and guide the RF lesions after transseptal access. Ablation lines were created as described by Pappone et al. [11,12] surrounding ipsilateral PVs at a minimum distance of 5 mm from their ostium by a thermocouple-equipped 8 mm tip catheter (Navistar, Biosense-Webster) at a target temperature of 55°C and a maximum output from 50 to 60 W. The end point was to reduce the amplitude of the endocardial potentials inside the encircled area below 0.15 mV.

Follow-up

Patients were followed in the outpatient clinic at 1, 4, 7 months and every 6 months thereafter if they remained asymptomatic. Routine 24-hours Holter monitoring was performed before each control and patients were also asked to communicate any symptom suggestive of recurrence between scheduled visits in order to document it. A transthoracic echocardiogram was also performed 4 months after ablation procedure. Acenocumarol was maintained at least for 3 months after the ablation. All patients received antiarrhythmic drugs (flecainide if no structural heart disease was diagnosed or amiodarone if there was evidence of structural heart disease) during the first month to control early recurrences. Drugs were withdrawn afterwards if patients remained free of recurrences.

A contrast enhanced MRA (1.5 T. Signa Horizon. GE Medical Systems) was routinely performed in all the patients submitted to an ablation procedure. A single radiologist blinded to the type and result of the procedure and clinical characteristics of patients evaluated the test. MRA was obtained 4 months after the ablation since progression of the stenosis is rare after this period of time [7,14]. A significant stenosis was considered with a diameter lumen reduction of >70%.

Statistical Analysis

Continuous variables are expressed as mean ± SD. Comparisons were made using the Student's *T*-test and Chi-square analysis. Recurrence-free was compared using the Kaplan-Meier survival curves with log rank test. Multivariate logistic regression analysis was performed to determine independent predictors of an event. Results with $p < 0.05$ were considered statistically significant.

Results

MRA was performed in 73 of 78 consecutive patients submitted to an AF ablation procedure. The MRA could not be done in 3 patients with claustrophobia, in a patient with a pacemaker and in another with an implantable automatic defibrillator. In 32 patients, the ablation was done with a SSOA approach; in 41 patients the ablation was done with the CPVA method. During a mean follow-up of 14.7 ± 12.1 months, 23 and 31 patients of SSOA and CPVA groups respectively were free from recurrences (72% vs 76% arrythmia free; long rank test $p =$ NS).

None of the patients developed symptoms suggestive of PV stenosis. However, in 6 patients a significant PV stenosis was detected in the routine MRA, all them in the SSOA group, none in the CPVA group (18.8% vs 0% of the evaluated patients; $p = 0.005$). In 4 patients, the stenosis was

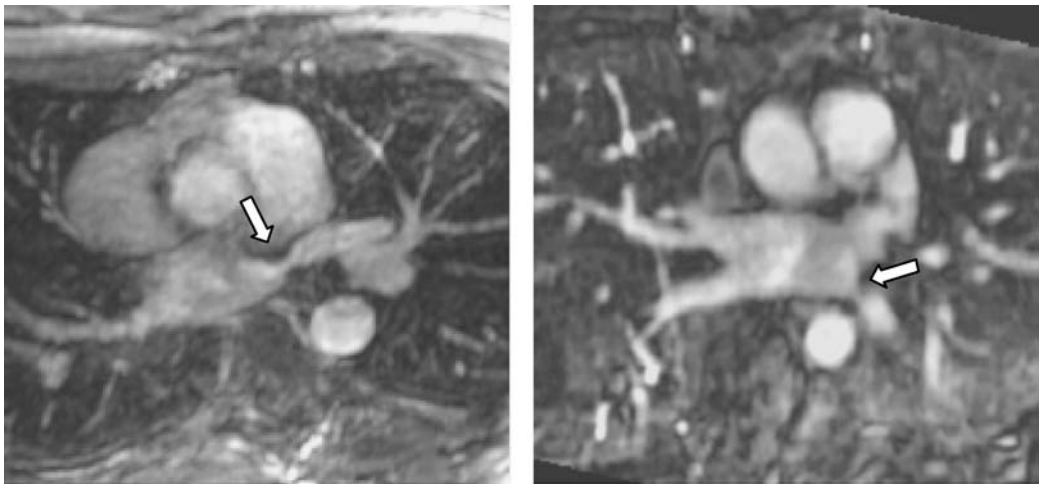

Fig. 1. *Two patients with pulmonary vein (PV) stenosis. Left and right images show left superior and left inferior PV stenosis respectively (arrows).*

located in the left superior PV (LSPV), in 1 patient at the left inferior PV (LIPV) and in 1 patient both the LSPV and the LIPV had a significant stenosis.

In the CPVA group, ablation lines encircled all PV's in all cases. In SSOA group a mean of 1.8 ± 0.7 PVs per patient were treated with a mean of 10.3 ± 0.8 minutes of radiofrequency application. Ostial segments where RF was applied to achieve the PV electrical disconnection were classified by anatomic and fluoroscopic guidance among 4 ostial divisions: anterior, posterior, superior and inferior segments. In our series, the earliest electrical activity was recorded on the inferior segment in the 57 and 58% of the treated LSPV and RSPV respectively (see Table 2). LSPV was isolated in the 93.8% of patients, LIPV in 18.8%, right superior PV (RSPV) in 59.4% and right inferior PV (RIPV) in 6.3%. A second procedure was necessary in 3 patients of the SSOA group due to AF recurrence, therefore the total number of PVs isolated were 33 LSPVs, 6 LIPVs, 21 RSPVs and 2 RIPVs. Overall, 15.2% of the LSPVs and 33.3% of the LIPVs treated by SSOA developed stenosis.

Table 2. *PV ostial segments in which RF energy was deployed in SSOA group*

	Inferior (%)	Posterior (%)	Superior (%)	Anterior (%)
LSPV ($n = 30$)	56.6	26.6	23.3	26.6
RSPV ($n = 19$)	57.9	26.3	21.0	21.0
LIPV ($n = 6$)	16.7	33.3	50.0	16.7
RIPV ($n = 2$)	0	0	100	100

PV: pulmonary vein. RF: radiofrequency. SSOA: selective segmental ostial ablation. LSPV: left superior PV. RSPV: right superior PV. LIPV: left inferior PV. RIPV: right inferior PV.

Fig. 2. *Example of anatomical variant of the pulmonary veins where a single ostium of both left and right sided was observed.*

No differences in patient characteristics or procedural details were found between patients with and without PV stenosis in SSOA group, and no predictors of stenosis could be identified.

In our series 16 patients (22% of the total) had some anatomical variant of the PVs, being the most common variant the presence of single ostium of the left PVs (15% of the patients) and the presence of 3 right PVs (5% of the patients; see Fig. 2).

Discussion

PV stenosis is a potential complication of AF ablation. Correlation between the technique employed

for the ablation and the incidence of PV stenosis has been studied by Saad et al. [7]. The authors suggest that the most important point is the accuracy of the technique for differentiating the real ostium of the PV. Therefore, different methods like venography, intracardiac ultrasonography and electroanatomic mapping are used to define more accurately the junction between the atrial wall and the PV [5–8]. Even with these techniques, in large series, stenosis persists as a complication ranging between 5 to 30% [14]. Some authors do not look systematically for PV stenosis in all patients and only if the patient becomes symptomatic, a diagnostic procedure is performed [15]; our results show that this method may underestimate the real incidence of this complication.

In our series, AF ablation was performed using two different approaches and the incidence of PV stenosis was compared. The absence of stenosis in the CPVA group correlates with the findings of the series published by Pappone et al. [3,12,13,16], and although there are reports of PV occlusion using this technique [17], the risk seems lower because of a better definition of the catheter position in respect of the PV ostium. Furthermore, in CPVA procedures RF is delivered at least 5 mm away from the defined ostium.

In our experience, all PV stenosis were found in the SSOA group and this is in part, due to the more difficult differentiation of the PV ostium and because of the need to apply energy close to the ostium, making it easier to produce a lesion inside the vein. Moreover, although the total amount of RF energy was higher in CPVA than in SSOA, a major concentration of RF lesions was required in SSOA technique in order to achieve the PV isolation, delivering the RF energy in a more limited region of the PV ostium. It is of interest that in the SSOA group the left sided PVs were more stenosed, and this correlates with previous reports in the literature [14]. A possible explanation may be that the ablation catheter moves easily inside the left sided veins with each breathing movement, thus delivering the energy inside the PV. In our approach, SSOA was performed treating only those PVs showing electrical activity, being the most commonly treated the LSPV and the RSPV. These results were in accordance with other studies where only arrythmogenic PVs were treated an could be explained because the muscular sleeves insertion into PVs was more developed in upper than in lower veins [1,2].

Recently, a study comparing the efficacy and safety of both ablation strategies in a series of 100 randomized patients has been published [18]. Multislice CT was routinely performed 3 months after the ablation procedure, and stenosis of at least 1 PV was found in 12 and 6% of the SSOA and CPVA patients respectively. This PV stenosis incidence is similar to our results in the SSOA group, however we had not observe any stenosis in the CPVA group. This discrepancy maybe due to the higher power limit output used in this study, up to 70 W in 8 mm tip or 50 W in cooled 4 mm tip catheter respectively.

All patients with PV stenosis in our series were asymptomatic, and were identified because MRA was sistematically performed. The development of clinical symptoms is associated with the number of PVs affected and the degree of narrowing [14]. Lung perfusion defects were seen in PV narrowing greater than 70% in the left PV [7]. When right PV are affected lung scan perfusion defects appear with somewhat lower degrees of stenosis ranging between 50 to 65%; this might be explained because of the lower pressure in the right PV that may increase the pressure gradient [19]. In our series there were no total occlusions, all but one patient had only one vein affected, and right sided veins were not involved, contributing to the absence of respiratory symptoms associated with found PV stenosis.

In this series, a single MRA was performed 4 months after the ablation procedure, so later PV stenosis progression could have been missed. However, although PV narrowing have not been exactly quantified because a previous MRA was not performed, all PV stenosis images we obtained showed a focalised and high degree narrowing that must be catalogued as severe ($>70\%$) in all cases. In the remaining patients, PVs ostium did not show appreciable alterations, and normal or mild narrowed ($<50\%$) PVs rarely progress beyond the third month [7,14]. Therefore, we decided not repeat MRA beyond the 4th month since the ablation procedure because of the low probability to observe new findings.

Conclusions

Pulmonary vein stenosis is a potential complication of the selective segmental ostial ablation of atrial fibrillation. The PV stenosis is seldom observed in circumferential pulmonary veins ablation approach. The study confirms that magnetic resonance angiography is useful for identifying patients with asymptomatic pulmonary vein stenosis and anatomical variants of the left atria.

References

1. 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 initiatied from multiple pulmonary venous foci. *Circulation* 2000;101:1409–1417.

2. Marrouche NF, Dresing T, Cole C, Bash D, Saad E, Balaban K, Pavia SV, Schweikert R, Saliba W, Abdul-Karim A, Pisano E, Fanelli R, Tchou P, Natale A. Circular mapping and ablation of the pulmonary vein for treatment of atrial fibrillation: Impact of different catheter technologies. *J Am Coll Cardiol* 2002;40:464–474.
3. 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.
4. Taylor GW, Kay GN, Zheng X, Bishop S, Ideker R et al. Pathological effects of extensive radiofrequency energy applications in the pulmonary veins in dogs. *Circulation* 2000;101:1736–1742.
5. Yu W, Hsu T, Tai C, Tsai CF, Hsieh MH, Lin WS, Lin YK, Tsao HM, Ding YA, Chang MS, Chen SA. Acquired pulmonary vein stenosis after radiofrequency ablation of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2001;12:887–892.
6. 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.
7. Saad E, Rossillo A, Saad C, 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 alter radiofrequency ablation of atrial fibrillation. Functional characterization, evolution and influence of the ablation strategy. *Circulation* 2003;108:3102–3107.
8. Scharf C, Sneider M, Case I, Chugh A, Lai SW, Pelosi F Jr, Knight BP, Kazerooni E, Morady F, Oral H. Anatomy of the pulmonary veins in patients with atrial fibrillation and effects of segmental ostial ablation analyzed by computed tomography. *J Cardiovasc Electrophysiol* 2003;14:150–155.
9. Yang M, Akbari H, Reddy GP, Higgins C et al. Identification of pulmonary vein stenosis after radiofrequency ablation for atrial fibrillation using MRI. *J Comput Assist Tomogr* 2001;25:34–35.
10. 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 the use of Magnetic Resonance Imaging. *Circulation* 2003;107:2004–2010.
11. 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.
12. 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. *J Am Coll Cardiol* 2003;42:185–197.
13. Silva RM, Mont L, Berruezo A, Fosch X, Wayar L, Alvarenga N, Chueca E, Brugada J. Radiofrequency ablation in the treatment of focal atrial fibrillation using circumferential mapping and segmentary disconnection of pulmonary veins. *Rev Esp Cardiol* 2003;56:361–367.
14. Saad E, Marrouche N, Saad C, 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.
15. Mansour M, Ruskin J, Keane D. Efficacy and safety of segmental ostial versus circumferential extra-ostial pulmonary vein isolation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2004;15:532–537.
16. Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G, Mazzone P, Tortoriello V, Landoni G, Zangrillo A, Lang C, Tomita T, Mesas C, Mastella E, Alfieri O. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation* 2004;109:327–334.
17. Vasamreddy C, Jayam V, Bluemke DA, Calkins H et al. Pulmonary vein occlusion: An unanticipated complication of catheter ablation of atrial fibrillation using the anatomic circumferential approach. *Heart Rhythm* 2004;1:78–81.
18. Karch MR, Zrenner B, Deisenhofer I, Schreieck J, Ndrepepa G, Dong J, Lamprecht K, Barthel P, Luciani E, Schomig A, Schmitt C. Freedom from atrial tachycardia after catheter ablation of atrial fibrillation. A randomized comparison between 2 current ablation strategies. *Circulation* 2005;111:2875–2880.
19. Firstenberg M, Greenberg N, Smedira N, Prior DL, Scalia GM, Thomas JD, Garcia MJ. Doppler echo evaluation of pulmonary venous-left atrial pressure gradients: Human and numerial model studies. *Am J Physiol* 2000;279:H594–H600.