Left Atrial Ablation Versus Biatrial Ablation for Persistent and Permanent Atrial Fibrillation

A Prospective and Randomized Study

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OBJECTIVES	The aim of this study was to compare—in patients with persistent and permanent atrial fibrillation (AF)—the efficacy and safety of left atrial ablation with that of a biatrial approach.
BACKGROUND	Left atrium-based catheter ablation of AF, although very effective in the paroxysmal form of the arrhythmia, has an insufficient efficacy in patients with persistent and permanent AF.
METHODS	Eighty highly symptomatic patients (age, 58.6 ± 8.9 years) with persistent (n = 43) and permanent AF (n = 37), refractory to antiarrhythmic drugs, were randomized to two different ablation approaches guided by electroanatomical mapping. A procedure including circumferential pulmonary vein, mitral isthmus, and cavotricuspid isthmus ablation was performed in 41 cases (left atrial ablation group). In the remaining 39 patients (biatrial ablation group), the aforementioned approach was integrated by the following lesions in the right atrium: intercaval posterior line, intercaval septal line, and electrical disconnection of the superior vena cava.
RESULTS	During follow-up (mean duration 14 ± 5 months), AF recurred in 39% of patients in the left atrial ablation group and in 15% of patients in the biatrial ablation group (p = 0.022). Multivariable Cox regression analysis showed that ablation technique was an independent predictor of AF recurrence during follow-up.
CONCLUSIONS	In patients with persistent and permanent AF, circumferential pulmonary vein ablation, combined with linear lesions in the right atrium, is feasible, safe, and has a significantly higher success rate than left atrial and cavotricuspid ablation alone. (J Am Coll Cardiol 2006;47: 2504–12) © 2006 by the American College of Cardiology Foundation

Recent clinical investigations have shown that the electrical isolation of the pulmonary vein (PV) tissue may reduce atrial fibrillation (AF) recurrences in up to 70% of patients with paroxysmal AF (1). However, the efficacy of this ablation technique in patients with prolonged forms of AF is rather low (1). Consequently, several other ablation approaches, characterized by a substrate modification other than PV ablation, have been proposed in persistent or permanent AF (2–8). Overall, such alternative ablation procedures seem to be more effective than PV isolation, even if their success rates appear extremely variable (2–8).

Experimental (9–19) and clinical (20–24) studies showed that the right atrium can be involved in the AF initiation and maintenance, and we recently found that a specific right atrial linear concept in combination with antiarrhythmic drugs was quite effective in treating drug-refractory AF (25). Furthermore, areas localized in both atria characterized by fragmented electrograms or rapid electrical activity (7,26) have shown to be critical in the AF persistence. Thus, taking into account these observations, we have hypothe-

sized that in prolonged forms of AF biatrial ablation could be more effective than left atrial ablation alone. Accordingly, aim of this prospective and randomized study was to compare—in patients with persistent and permanent AF— the efficacy and safety of left atrial ablation, combined with cavotricuspid isthmus ablation, with that of a biatrial approach, including left atrial catheter ablation and linear lesions in the right atrium. When possible, the predetermined lesions were performed along sites of fractionated electrograms or rapid electrical activity.

METHODS

Study subjects. Eighty consecutive patients (28 women, 58.6 ± 8.9 years) undergoing radiofrequency catheter ablation for symptomatic, persistent (43 patients) or permanent AF (37 patients), were enrolled in the study. Inclusion criteria were: 1) AF resistant to more than three attempts of pharmacological and/or electrical cardioversion; or 2) recurrent, persistent AF despite prophylaxis with at least three different antiarrhythmic drugs (class I and/or III). Atrial fibrillation was defined as persistent when lasting more than seven days and as permanent AF when resistant to cardioversion or relapsing within 24 h (27). The clinical characteristics of the patients are shown in Table 1.

Study protocol. The study was planned as a prospective, open, and randomized trial with parallel groups. The study

protocol was approved by the ethics committee of our institution. Eligible patients were assigned to one of the two study arms immediately before the ablation procedure according to a computer-generated randomization list. All patients were informed of the investigational nature of the procedure and provided written informed consent before being included in the study and randomized.

According to randomization, 41 patients underwent circumferential ablation plus mitral and cavotricuspid isthmus ablation (left atrial ablation group), while 39 patients underwent biatrial ablation. Sixty-seven patients had structural heart disease. The clinical characteristics of the patients in the two groups were similar (Table 1).

To enhance the likelihood of maintaining sinus rhythm, oral amiodarone was administered in all the patients who had no contraindication to the drug. In this last case, alternative drugs were used (sotalol, flecainide, propafenone). All patients were thus on antiarrhythmic drugs during the procedure (Table 1). Forty-two patients (20 persistent and 22 permanent) were on amiodarone when the ablation has been performed. The antiarrhythmic therapy was discontinued six months after the procedure. After this period, the decision to continue antiarrhythmic medications was based on AF occurrence or the presence of frequent and/or repetitive atrial ectopic beats. After the ablation, patients were treated with low-molecular-weight heparin for four to six days and placed on anticoagulant therapy. After six months, in the absence of AF recurrences, anticoagulant treatments were discontinued, unless other major risk factors were present. Follow-up consisted of outpatient visits, echocardiography, and Holter monitoring performed one and three months after the ablation procedure and, subsequently, every three months, or in case of occurrence of any clinical symptom. All patients were instructed to regularly assess their pulse and to confirm on electrocardiogram (ECG) any suspected recurrence of arrhythmia. Transesophageal echocardiography was performed three months after ablation to assess potential PV narrowing.

The primary end point of the study was the time to the first recurrence of AF during follow-up. Atrial fibrillation recurrence was defined as any electrocardiographically confirmed episode of AF lasting >30 s. After an episode of AF, formal study participation ended, and the patient was withdrawn from any further analysis. Time to AF recurrence was computed as the number of days between the ablation procedure and the electrocardiographic confirmation of the arrhythmia. As the episodes of AF occurring within the first few weeks after ablation are usually transient, any event taking place within the first six weeks of follow-up was excluded from the analysis (7). Actually, 9 of the 41 (22%) patients in the left atrial group and 5 of the 39 (13%) in the biatrial group had AF recurrence during the first six weeks of follow-up.

Mapping and ablation procedure. Two quadripolar standard catheters were placed in the coronary sinus (CS) and in the right ventricle. After transseptal catheterization, heparin was titrated to maintain an activated clotting time of 250 to 300 s. A special deflectable 8-mm tip catheter (NAVISTAR, Biosense-Webster, Diamond Bar, California) was used for mapping and ablation. Real-time three-dimensional left atrial and right atrial maps were reconstructed using a nonfluoroscopic mapping system (CARTO, Biosense-Webster). The mapping procedure was performed during AF. Maps were acquired to assess amplitude of local atrial electrograms. Areas of fractionated atrial electrograms or rapid atrial activity were tagged on the three-dimensional maps. When possible, the predetermined lesions were performed both in left and right atrium along these sites, tagged as multiple fractionated atrial electrograms or rapid activity (7,26). Fractionated atrial electrograms were defined as atrial electrograms composed of two deflections or more, and/or perturbation of the baseline with continuous deflection of a prolonged activation complex over a 10-s recording period (26). Rapid activity was defined as atrial electrograms with a very short cycle length (≤120 ms) averaged over a 10-s recording period (26).

Radiofrequency power was titrated to achieve a temperature of 50°C to 60°C for 20 to 60 s (maximum power of 80 W) for each single lesion to reduce the local peak-to-

Table 1. Clinical Characteristics of Patients Who Underwent Biatrial Ablation and Left Atrial Ablation

	Biatrial Ablation (n = 39)	Left Atrial Ablation (n = 41)	p Value
Age, yrs	57.9 ± 8.9	59.2 ± 9.1	0.6
Gender, M/F, n	26/13	26/15	0.8
Duration of atrial fibrillation, yrs	8 ± 3	7 ± 4	0.3
Persistent atrial fibrillation, n	19	24	0.4
Permanent atrial fibrillation, n	20	17	0.4
Structural heart disease, n	33	34	0.9
Hypertension, n	16	18	1.0
Coronary artery disease, n	8	9	0.9
Idiopathic DC, n	5	4	0.9
Valvular disease, n	4	3	0.9
Left atrial diameter, mm	50.8 ± 5	51.1 ± 5	0.5
LV ejection fraction, %	50.2 ± 7.8	51.2 ± 7.4	0.6
AAD during the procedure			
Amiodarone	20	22	0.9
Sotalol	9	8	0.9
Class 1C	10	11	0.9

Data are shown as mean ± SD in case of continuous variables; in case of categorical variables, the number of patients (n) is reported.

AAD = antiarrhythmic drugs; DC = dilated cardiomyopathy; LV = left ventricular.

peak bipolar electrogram amplitude by $\geq 80\%$ or <0.1 mV. When there was a $>80\%$ decrease in the local electrogram amplitude or when energy had already been applied for 60 s, the catheter was moved to the next site. Left atrial ablation consisted of: 1) circumferential lines performed ≥ 1 cm from the PV ostia; and 2) connection from the inferior portion of left inferior encircling lesion to the mitral annulus (mitral isthmus). After completion of the encircling lesions, additional applications of radiofrequency energy were delivered within the circles at sites where the local electrogram amplitude was ≥ 0.1 mV (maximum power output to 50 W and target temperature to 50°C). The end point of the procedure was the completion of the proposed circular and linear lesions, whereas neither definite isolation of the PV nor complete block along the lines was a required prerequisite of the procedure. Cavotricuspid isthmus ablation was then performed to achieve a bidirectional conduction block.

In the patients who underwent biatrial ablation, the following lesions, other than cavotricuspid isthmus ablation, were added in the right atrium: 1) a posterior intercaval line; 2) a septal line from the septal portion of the superior vena cava to the fossa ovalis, proceeding to the CS ostium where a circumferential line around the ostium was performed, particularly burning the posteroseptal area just behind the ostium, and then the line terminates in the inferior vena cava; and 3) the electrical disconnection of the superior vena cava from the right atrium (25). The isolation of the superior vena cava was performed in all patients during sinus rhythm (target, 50°C with a power limit of 40 W). To avoid phrenic nerve injury, just before radiofrequency delivery, high amplitude stimulation was performed during disconnection of superior vena cava. The proximal His bundle was tagged on the CARTO map and the mid-portion of the septal line and the portion around CS was performed—if possible—in sinus rhythm, to avoid atrioventricular node damage.

When AF was terminated during ablation, we did not re-induce AF, and the procedure was continued, until all the predetermined linear lesions were completed. In all patients we have determined the atrial fibrillation cycle length (AFCL) within CS: 1) before ablation; 2) after left atrial ablation; and 3) after right atrial ablation in those patients randomized to this arm of the study. If AF terminated during ablation, the AFCL was determined before termination. The measurements were performed as published by Haïssaguerre et al. (28).

Statistical analysis. Means ($\pm$ SD) were calculated for continuous variables, while frequencies were measured for categorical variables. Distributions of continuous variables were determined by the Kolmogorov-Smirnov test, and all were found to be non-normal. Group differences for continuous data were then examined by the Mann-Whitney two-sample test. In case of categorical variables, group differences were examined by chi-square or Fisher exact test as appropriate. In particular, the Fisher exact tests was

applied in case of an expected frequency of <5. A value of $p < 0.05$ was considered significant.

The primary analysis of outcomes was by intention to treat. The recurrence of AF in the two treatment groups was tested with the odds ratio of the two-binomial proportion analysis. Sample size calculation was based on an expected 20% per year recurrence rate of AF in the biatrial ablation arm and on an expected 50% per year recurrence rate in the left atrial ablation arm. Consequently, with an alpha level of 0.05 and a test power of 0.80, the resulting sample size was 40 patients in each treatment group.

The cumulative risk of recurrence of AF within each group was estimated by means of the Kaplan-Meier method. The survival curves of the two different treatment groups were then formally compared by use of the log-rank test. The Cox proportional hazards regression method was used to determine the relationship of clinical characteristics to the recurrence of AF during follow-up. The following variables, determined from the baseline evaluation, were considered potential predictors of recurrence of AF: age, gender, left atrial dimensions, structural heart disease, left ventricular ejection fraction, treatment group, and presence of permanent AF before the ablation procedure. Besides, the continuation of antiarrhythmic medications after six months from the ablation procedure was also entered in the Cox model as a time-dependent covariate. Variables were then analyzed in a stepwise fashion to develop Cox models of the study end point. Data analysis was performed using the SPSS statistical software package (version 12.0, SPSS Inc., Chicago, Illinois).

RESULTS

Procedural data. All patients were in AF at the beginning of ablation, and all of them completed the planned interventional procedure. In the left atrial ablation group, the mean procedure and fluoroscopy duration was 164 ± 25 min and 31 ± 10 min, respectively, while the mean total duration of radiofrequency energy applications was 44 ± 12 min. In the biatrial ablation group, the mean procedure and fluoroscopy duration was 228 ± 32 min ($p < 0.001$ vs. left atrial ablation group) and 41 ± 14 min ($p = 0.0005$ vs. left atrial ablation group), respectively, while the mean total duration of radiofrequency energy applications was 63 ± 16 min ($p < 0.001$ vs. left atrial ablation group). The mean power and temperature during ablation was similar in the left atrial ablation group and in the biatrial ablation group (36 ± 14 W and 37 ± 15 W, respectively; 51 ± 6°C and 49 ± 7°C, respectively).

Atrial fibrillation terminated during ablation in 43 cases (53%), 10 of 41 patients (24%) in the left atrial ablation group and 33 of 39 patients (85%) in the biatrial ablation group ($p < 0.0001$). Of these 43 patients, AF converted to sinus rhythm in 35 cases, to typical atrial flutter in 3 patients, and to atypical atrial flutter in 5 cases.

In the biatrial ablation group, the AF terminated in the left atrium in 9 cases and in the right atrium in the remaining 24 cases. A gradual organization of atrial electrograms and a progressive increase of atrial cycle length preceded sinus rhythm restoration (Fig. 1). A significant increase in AFCL was found after left atrial ablation (172 ± 11 ms to 199 ± 12 ms; p < 0.001). The AFCL prolonged further in the patient who underwent right atrial ablation (199 ± 12 ms to 235 ± 19 ms; p < 0.001). This increase was significantly greater in patients with sinus rhythm restoration during ablation compared with those with persistence of AF after ablation (174 ± 9 ms to 221 ± 14 ms vs. 170 ± 12 ms to 247 ± 15 ms), representing an increase of 77 ± 19 versus 48 ± 11 (p < 0.001). In the 37 patients (47%) in whom the ablation procedure was not associated with sinus rhythm restoration, AF was terminated by ibutilide (15 patients) or by electrical cardioversion (22 patients).

The post-ablation voltage maps revealed the absence of discrete electrical activity (voltage <0.1 mV) at all sites inside the lesions and just around ablation lines in all patients of both groups (Fig. 2). The electrical disconnection of the superior vena cava was obtained in all patients who underwent biatrial approach.

The number of radiofrequency applications required to isolate the superior vena cava was 2.5 ± 1.2 (range 2 to 12). The mean total radiofrequency energy application was 79 ± 43 s (range 38 to 212 s).

Clinical outcome. Patients were followed for 14 ± 5 months, and the follow-up period was not different in the two study groups (13 ± 6 months in the left atrial ablation group and 15 ± 5 months in the biatrial ablation group). Atrial fibrillation recurred in 16 of 41 patients (39%) in the left atrial ablation group after a mean time of 3.0 ± 1.5 months and in 6 of 39 patients (15%) in the biatrial ablation group after a mean time of 3.9 ± 2.3 months (odds ratio 0.284; 95% confidence interval [CI] 0.100 to 0.812, p = 0.034). The Kaplan-Meier actuarial estimates of AF recurrence after 3, 6, and 18 months were 12.8%, 15.4%, and 15.4% in the biatrial ablation group and 24.4%, 34.1%, and
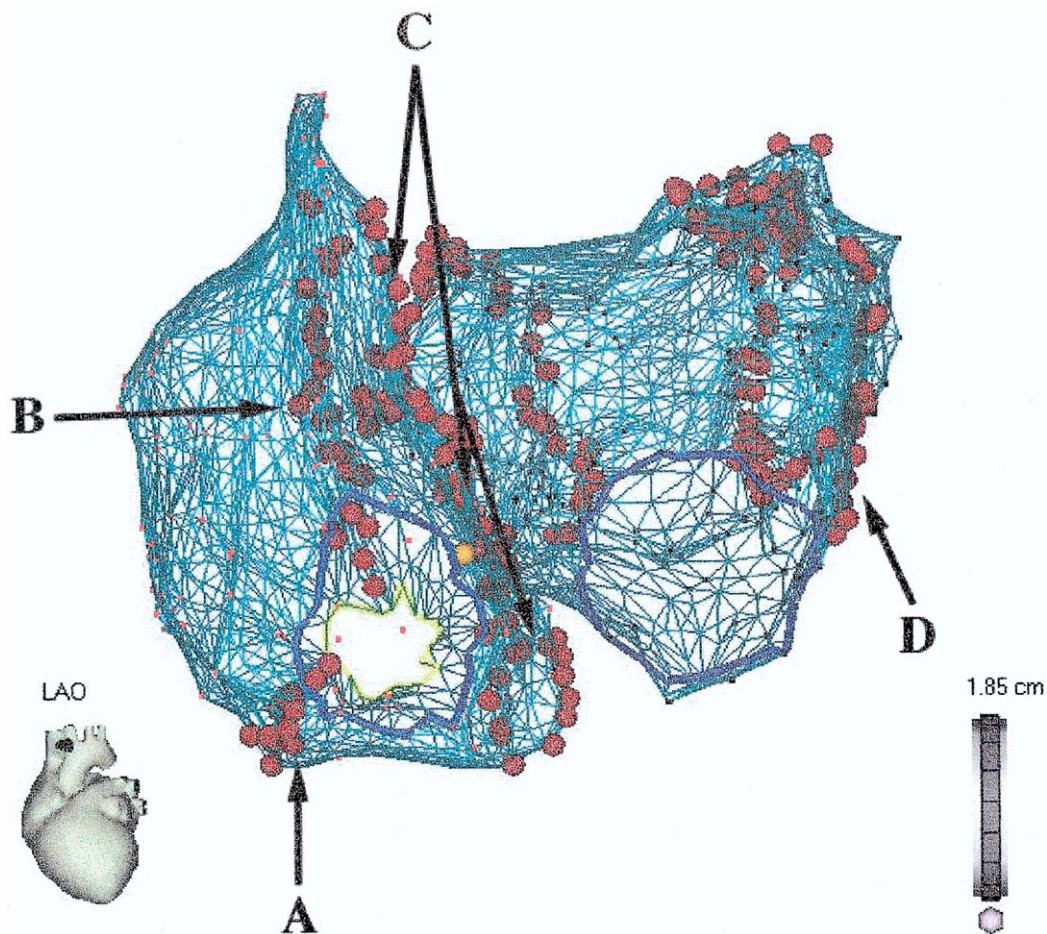

Figure 1. Intended line designs: anteroposterior of a mesh graph of the electroanatomic reconstruction of the right and the left atrium. Multiple **dark red dots** represent ablation lines. The following lesions were performed in the right atrium: **(A)** the isthmus line between the tricuspid annulus and the inferior vena cava. **(B)** The posterior intercaval line. **(C)** The septal line that begins from the superior vena cava, proceeds to the fossa ovalis, and to the coronary sinus ostium where a circumferential line was performed, and terminates in the inferior vena cava. In the left atrium, a circumferential lesion was placed around the left and right pulmonary veins. In addition, a linear lesion connecting the left circular lesion with the mitral annulus was placed **(D)**. LAO = left anterior oblique.
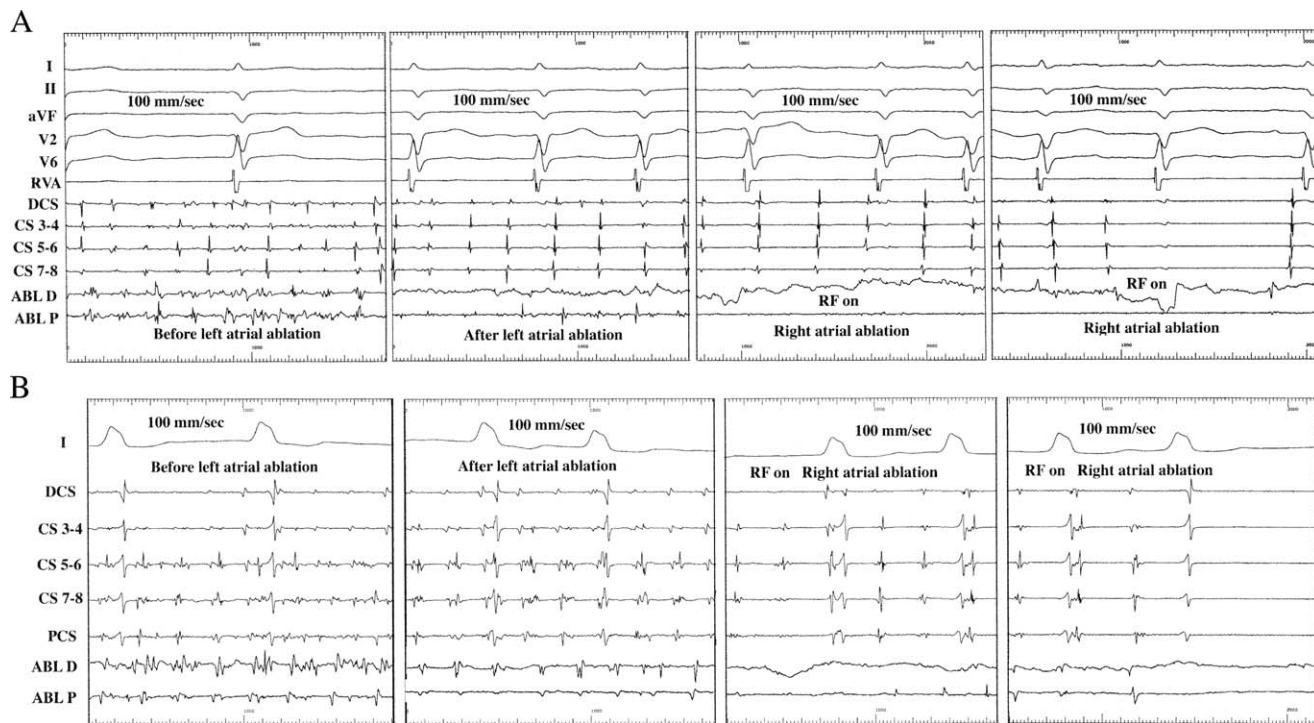
Figure 2. Examples of termination of atrial fibrillation during radiofrequency (RF) application in two patients **(A and B)** with permanent atrial fibrillation. Both patients had failure of electric cardioversion. Note that the atrial fibrillation termination occurred in both patients during right atrial ablation (septal line) after progressive prolongation of cycle length of FF intervals. ABL D = distal ablation catheter; ABL P = proximal ablation catheter; CS = coronary sinus; DCS = distal coronary sinus; PCS = proximal coronary sinus; RVA = right ventricular apex.

39% in the left atrial ablation group (log-rank p = 0.022) (Fig. 3).

After six months of follow-up, 21 of 41 in the left atrial group, and 18 of 39 patients in the biatrial group were continued on antiarrhythmic drugs after the initial six months and for the remainder of follow-up. In the interval between six months and the end of follow-up, 23 of the 80 patients (7 in the left atrial and 16 in the biatrial group) were AF free without antiarrhythmic therapy. Figure 4 shows the success rates with and without antiarrhythmic drugs in the two groups. Table 2 shows the effect of antiarrhythmic drugs in patients with persistent and permanent AF who underwent biatrial and left atrial ablation. Twenty-one of the 22 patients with AF recurrence were on antiarrhythmic drug therapy.

In the multivariate Cox regression analysis, after adjustment for age, gender, left atrial dimensions, structural heart disease, type of AF (persistent vs. permanent), and continuation of antiarrhythmic therapy after six months from the ablation procedure, the ablation technique (biatrial ablation) was found to be an independent negative predictor of AF recurrence (hazard ratio of 0.223, 95% CI 0.80 to 0.623, p = 0.004). Moreover, a left ventricular ejection fraction <45% was found to be an independent positive predictor of AF recurrence (hazard ratio of 5.162, 95% CI 2.009 to 13.262, p = 0.001).

Complications. Two major complications were observed soon after the procedure: a retroperitoneal hematoma and an hemothorax (both patients were in the left atrial ablation

group). Six patients (four in the biatrial ablation group) developed atypical atrial flutter in the first three weeks after ablation. Additional ablation was not required in these patients because the arrhythmia was spontaneously self-terminating during the six-week blanking period.

DISCUSSION

Main findings. In this study, conducted in 80 symptomatic patients with either persistent and permanent AF, most with structural heart disease, the following were observed: 1) biatrial ablation was superior to left atrial ablation in maintaining patients free of AF recurrence during 14 ± 5 months (15% vs. 39% of AF recurrence); 2) the total procedure time was increased by the biatrial ablation of ~1 h in comparison with left atrial ablation; 3) complications were rare and uniformly present in the two arms of our study; and 4) the ablation technique and the ejection fraction were found by multivariate analysis to be independent predictor of AF recurrence.

Previous studies. Few and conflicting data have been reported about the effects of catheter ablation in persistent and permanent AF (1,26,29,30). Swartz et al. (29) had a success rate up to 90%, but a 22% incidence of major complications, by performing biatrial linear lesions in patients with chronic AF. Additional studies operating a compartmentalization of the right atrium and/or left atrium generally showed a low success rate in chronic AF (31,32). Subsequently, several studies pointed to the importance of
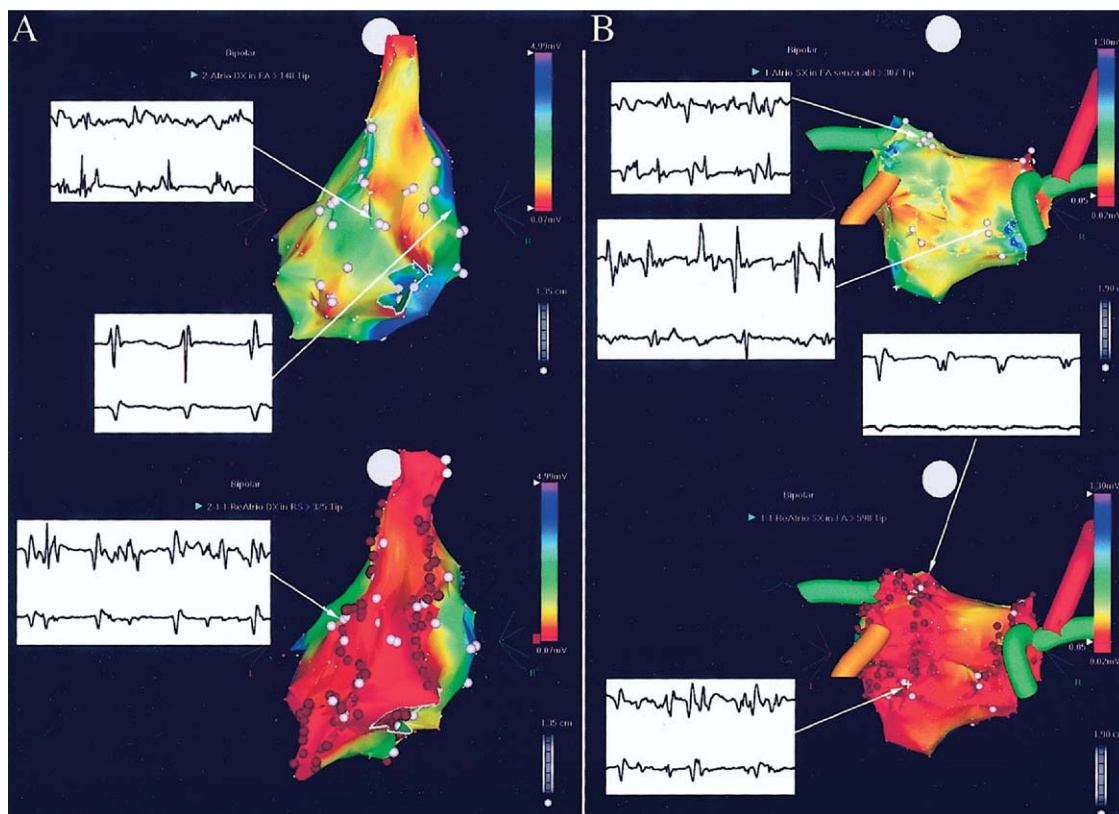
Figure 3. Voltage maps of the right **(A)** and left atrium **(B)** before ablation **(top)** and after ablation **(bottom)** (posteroanterior view). **Red** represents lowest voltage and **blue** and **purple**, highest voltage. Multiple **dark red dots** represent ablation lines. **Pink dots** represent area of complex fractionated electrograms. Electrograms recorded from distal electrode pairs **(upper tracing)** and proximal electrode pairs **(bottom tracing)** of ablation catheter in different areas of the right and left atrium are also shown.

the PVs as a critical area for the initiation and maintenance of AF (1,4,33). Haïssaguerre et al. (30) showed ~60% long-term success after PV isolation in patients with chronic AF. On the contrary, Oral et al. (1) reported that persistent AF usually is not eliminated by PV disconnection (22% of patients AF free). This finding is consistent with two surgical studies in which PV isolation maintained sinus rhythm in 33% (34) and 20% of patients (35). Recently, Hsu et al. (2) demonstrated a higher success rate (70% to 80%) in patients with persistent and permanent AF by the addition of left atrial ablation lines and cavotricuspid isthmus ablation to PV disconnection, and using the prevention of AF inducibility as other target of the ablative procedure (28), even if a repeated ablation was necessary in approximately 50% of patients. A different kind of approach (26), in which the complex fractionated electrograms recorded during AF in both atria were the target sites for catheter ablation, obtained stable sinus rhythm in 70% of patients with chronic AF at one-year follow-up after a single ablative session. The antral or circumferential ablation of PV was reported to be effective in approximately 70% of patients with chronic AF (4,5). In the present study, the success rate of PV encircling combined with the left isthmus and the cavotricuspid isthmus ablation was lower. However, results similar to ours have been reported by other studies (6,8,36). Ernst et al. (8) had a success of 58% in patients mostly with

paroxysmal AF. Karch et al. (36) observed in drug-resistant AF (43 paroxysmal and 7 persistent AF) after PV encircling a success rate at six months of 42% using seven-day Holter monitoring and 54% basing on arrhythmia-related symptoms. Kottkamp et al. (6), after circular plus linear left atrial lesions in persistent AF, showed freedom from AF in 38% of patients evaluated with 24-h Holter monitoring and 22% with seven-day ECG.

In our study, the prevalence of atypical atrial flutter (7% acute, 0% long term) was lower than other studies (6,7). It can be hypothesized that, in our patients, both the additional lesions in the right atrium and the use of antiarrhythmic drugs for at least six months have reduced the incidence of atypical atrial flutter and favored its spontaneous termination. Also, it is possible that in other studies the creation of several linear lesions in the left atrium (such as roof and posterior lines), often incomplete, more frequently led to gap-related atrial flutter.

Potential mechanisms of the efficacy of the combined left and right atrial ablation. A significant difference in the electrical activity was found between patients with chronic and paroxysmal AF (9,10). Lazar et al. (9) demonstrated that a left-to-right atrial frequency gradient exists for paroxysmal but not for persistent AF and postulated that the maintenance of persistent or chronic AF may be less dependent on posterior left atrium. Recently, Sanders et al.
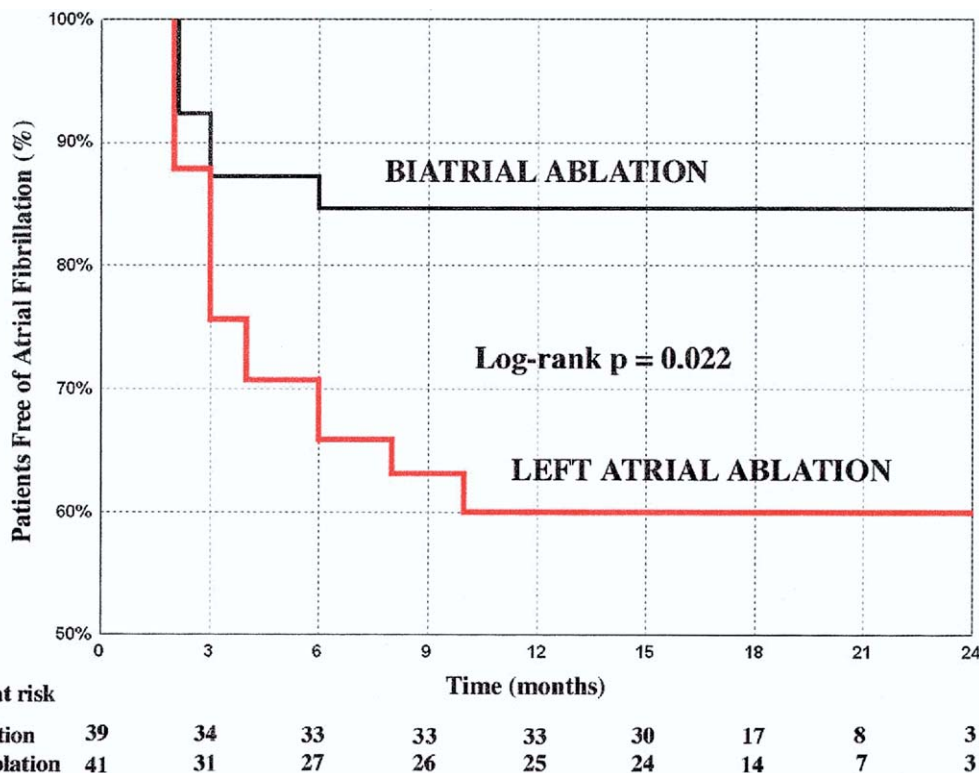
Figure 4. Kaplan-Meier estimate of survival free of atrial fibrillation after biatrial ablation **(solid line)** and left atrial ablation **(dotted line)**.

(37) observed that in patients with paroxysmal AF dominant sources of activity are often localized to the PVs, and, in contrast in patients with permanent AF, these dominant frequency sites are more often localized to the atria, including right atrial sites (37).

Combined left and right atrial linear ablation has been shown to eliminate chronic AF in animal models (11–15) and, specifically, two experimental studies demonstrated that biatrial ablation is more effective than right and left

Table 2. Success Rates With and Without Antiarrhythmic Drugs in Patients With Persistent and Permanent Atrial Fibrillation Who Underwent Biatrial and Left Atrial Ablation

	Biatrial Ablation (n = 39)	Left Atrial Ablation (n = 41)	p Value
Persistent atrial fibrillation, n	19/39 (49%)	24/41 (59%)	0.4
Unsuccessful, n	2/19 (11%)	8/24 (33%)	0.2
Successful without drugs, n	9/19 (47%)	5/24 (21%)	0.1
Successful with drugs, n	8/19 (42%)	11/24 (46%)	0.9
Amiodarone, n	2/8 (25%)	4/11 (36%)	0.7
Sotalol, n	2/8 (25%)	3/11 (28%)	0.9
Class 1C, n	4/8 (50%)	4/11 (36%)	0.8
Permanent atrial fibrillation, n	20/39 (51%)	17/41 (41%)	0.4
Unsuccessful, n	4/20 (20%)	8/17 (47%)	0.3
Successful without drugs, n	7/20 (35%)	2/17 (12%)	0.1
Successful with drugs, n	9/20 (45%)	7/17 (41%)	0.4
Amiodarone, n	4/9 (45%)	3/7 (42%)	0.9
Sotalol, n	2/9 (22%)	2/7 (29%)	0.6
Class 1C, n	3/9 (33%)	2/7 (29%)	0.9

atrial ablation alone to cure chronic AF (14,15). In humans, the Maze procedure, characterized by lesions in both atria, was effective in maintaining sinus rhythm in 99% of patients with chronic AF (38). Subsequently, surgical studies showed that lesions confined to the posterior part of the left atrium were effective, but with a lower percentage of success, in eliminating AF (34,35,39).

In our experience, a specific right atrial linear concept was effective with antiarrhythmic drugs in 66% of patients with refractory AF (25). The rationale for our approach in the right atrium was to create lesions in areas that seem to be critical in the maintenance and/or the induction of AF. In fact, the posterior and the septal wall have shown conduction deterioration, increased non-uniform anisotropy, and disorganized electrical activity (10,16,17,20,26). The septal line performed at the level of the interatrial connections have been shown to be highly effective in experimental studies (18,19,40). In humans, the CS was found to be a source of rapid repetitive electrical activity, and the electrical disconnection of the CS from the left atrium reduced the inducibility of sustained AF (41). In patients with AF and rheumatic heart disease, the ablation performed near the CS ostium was effective in 70% of cases (21). Also, Cox et al. (38) considered the cryoablation of CS as one of the most important steps in the surgical therapy of AF. Moreover, the right atrium is rarely the source of AF (22,23). Natale et al. (22) reported that 37.5% of chronic AF patients had right-sided foci. Furthermore, right atrial re-entrant arrhythmias determining AF have been reported, and short

lines of ablation lesion were effective in the cure of AF in these cases (24). Finally, the linear lesions performed in the posterior wall, inside the superior vena cava, and behind the CS ostium, other than in the posterior wall of the left atrium, could affect vagal enervation. In fact, these areas contain the largest populations of cardiac ganglia (42), and ablation of atrial parasympathetic nerve system demonstrated the abolishment of vagally mediated AF in dogs (43).

Furthermore, the success of the procedure can be, at least in part, related to the elimination of critical areas of slow conduction and/or pivot points by the ablation of complex fractionated electrograms found in both right and left atrium (7,26).

Study limitations. This study has some limitations. The first limitation is that asymptomatic paroxysmal AF may have recurred in some patients. In fact, the clinical efficacy was based on symptoms and on ambulatory monitoring performed every three months. However, considering that the study is randomized, the eventual asymptomatic recurrences could be expected to be equally distributed in both groups. Another limitation is that none of the patients with relapse of AF was submitted to a second ablation procedure. Therefore, we are not able to determine the possible reasons for AF recurrences in these patients and to assess the potential increase of the success rate after a second procedure. Moreover, it is quite possible that recurrence rate would have been higher in both groups had drug therapy been stopped in all patients at six months. Furthermore, many of our patients continued antiarrhythmic drugs (including amiodarone). This should be considered, when the patient desires AF catheter ablation to stop antiarrhythmic drugs. An additional potential limitation is that the efficacy of left-sided ablation alone may have been enhanced by using electrophysiologic end points such as elimination of PV potentials and demonstration of lines of block. Finally, complete PV isolation probably can further reduce the incidence of atypical atrial flutter (44).

Conclusions. This study first demonstrates that, in patients with persistent and permanent AF, the addition of multiple linear lesions in the right atrium to circumferential PV ablation determines a significant higher success rate than circumferential PV and cavotricuspid isthmus ablation alone. The biatrial approach showed to be feasible, safe, and effective in modifying the right and left AF substrate. The combination of right atrial linear lesions with the PV encircling can avoid the need of additional lines in the left atrium, which are technically challenging, potentially proarrhythmic, increase the risk of serious complications, and may impair the left atrial contractility.

If these preliminary data will be confirmed in randomized trials with larger population and longer follow-up, in patients with a prevalent substrate-mediated AF, the biatrial approach could be the treatment of choice.

REFERENCES

1. Oral H, Knight BP, Tada H, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002;105: 1077–81.
2. Hsu LF, Jais P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. N Engl J Med 2004;351:2373–83.
3. Jais P, Hocini M, Hsu LF, et al. Technique and results of linear ablation at the mitral isthmus. Circulation 2004;110:2996–3002.
4. Pappone C, Oreto G, Rosanio S, et al. 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;104:2539–44.
5. Marrouche NF, Dresing T, Cole C, et al. Circular mapping and ablation of the pulmonary vein for the treatment of atrial fibrillation. Impact of different catheter technologies. J Am Coll Cardiol 2002;40: 464–74.
6. Kottkamp H, Tanner H, Kobza R, et al. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions. Trigger elimination or substrate modification: early or delayed cure? J Am Coll Cardiol 2004;44:869–77.
7. Oral H, Chugh A, Lemola K, et al. Noninducibility of atrial fibrillation as an end point of left atrial circumferential ablation for paroxysmal atrial fibrillation. A randomized study. Circulation 2004; 110:2797–801.
8. Ernst S, Ouyang F, Lober F, Antz M, Kuck KH. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation. An electroanatomic study. J Am Coll Cardiol 2003;42:1271–82.
9. Lazar S, Dixit S, Marchlinski FE, Callans DJ, Gerstenfeld EP. Presence of left-to-right atrial frequency gradient in paroxysmal but not persistent atrial fibrillation in humans. Circulation 2004;110: 3181–6.
10. Gaita F, Calò L, Riccardi R, et al. Different patterns of atrial activation in idiopathic atrial fibrillation: simultaneous multisite atrial mapping in patients with paroxysmal and chronic atrial fibrillation. J Am Coll Cardiol 2001;37:534–41.
11. Elvan A, Huang X, Pressler ML, Zipes DP. Radiofrequency catheter ablation of the atria eliminates pacing-induced sustained atrial fibrillation and reduces connexin 43 in dogs. Circulation 1997;96:1675–85.
12. Mitchell MA, McRury ID, Haines DE. Linear atrial ablations in a canine model of chronic atrial fibrillation. Morphological and electrophysiological observations. Circulation 1998;97:1176–85.
13. Avitall B, Urbonas A, Urboniene D, Rozmus G, Helms R. Linear lesions provide protection from atrial fibrillation induction with rapid atrial pacing. J Cardiovasc Electrophysiol 2002;13:455–62.
14. Roithinger FX, Steiner PR, Goseki Y, Sparks PB, Lesh MD. Electrophysiologic effects of selective right versus left atrial linear lesions in a canine model of chronic atrial fibrillation. J Cardiovasc Electrophysiol 1999;10:1564–74.
15. Zarse M, Deharo JC, Mast F, Allessie MA. Importance of right and left atrial dilation and linear ablation for perpetuation of sustained atrial fibrillation. J Cardiovasc Electrophysiol 2002;13:164–71.
16. Papageorgiou P, Monahan K, Boyle NG, et al. Site-dependent intra-atrial conduction delay: relationship to initiation of atrial fibrillation. Circulation 1996;94:384–9.
17. Platonov PG, Yuan S, Hertervig E, et al. Further evidence of localized posterior interatrial conduction delay in lone paroxysmal atrial fibrillation. Europace 2001;3:100–7.
18. Tondo C, Scherlag BJ, Otomo K, et al. Critical atrial site for ablation of pacing-induced atrial fibrillation in the normal dog heart. J Cardiovasc Electrophysiol 1997;8:1255–65.
19. Betts TR, Roberts PR, Morgan JM. Feasibility of a left atrial electrical disconnection procedure for atrial fibrillation using transcatheter radiofrequency ablation. J Cardiovasc Electrophysiol 2001;12:1278–83.
20. Gaita F, Riccardi R, Calò L, et al. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation. Electrophysiological findings and ablation results. Circulation 1998;97:2136–45.

21. Nair M, Shah P, Batra R, et al. Chronic atrial fibrillation in patients with rheumatic heart disease. Mapping and radiofrequency ablation of flutter circuits seen at initiation after cardioversion. Circulation 2001; 104:802–9.

22. Natale A, Pisano E, Beheiry S, et al. Ablation of right and left atrial premature beats following cardioversion in patients with chronic atrial fibrillation refractory to antiarrhythmic drugs. Am J Cardiol 2000;85: 1372–5.

23. Lin WS, Tai CT, Hsieh MH, et al. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. Circulation 2003;107:3176–83.

24. Liu TY, Tai CT, Chen SA. Treatment of atrial fibrillation by catheter ablation of conduction gaps in the crista terminalis and cavotricuspid isthmus of the right atrium. J Cardiovasc Electrophysiol 2002;13: 1044–6.

25. Caló L, Lamberti F, Loricchio ML, et al. Long-term follow-up of right atrial ablation in patients with atrial fibrillation: efficacy and impact of a hybrid approach on quality of life. J Cardiovasc Electrophysiol 2004;15:37–43.

26. Nademanee K, McKenzie J, Kosar E, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. J Am Coll Cardiol 2004;43:2044–53.

27. Levy S, Camm AJ, Saksena S, et al. International consensus on nomenclature and classification of atrial fibrillation. Europace 2003;5: 119–22.

28. Haïssaguerre M, Sanders P, Hocini M, et al. Changes in atrial fibrillation cycle length and inducibility during catheter ablation and their relation to outcome. Circulation 2004;109:3007–13.

29. Swartz JF, Pellersels G, Silvers J, Patten L, Cervantes D. A catheter-based curative approach to atrial fibrillation in humans (abstr). Circulation 1994;90 Suppl 1:I335.

30. Haïssaguerre M, Jais P, Shah DC, et al. Catheter ablation of chronic atrial fibrillation targeting the reinitiating triggers. J Cardiovasc Electrophysiol 2000;11:2–10.

31. Maloney JD, Milner L, Barold S, Czerska B, Markel M. Two-staged biatrial linear and focal ablation to restore sinus rhythm in patients with refractory chronic atrial fibrillation: procedure experience and follow-up beyond 1 year. Pacing Clin Electrophysiol 1998; 21:2527–32.

32. Ernst S, Schlüter M, Ouyang F, et al. Modification of the substrate for maintenance of idiopathic human atrial fibrillation: efficacy of radiofrequency ablation using nonfluoroscopic catheter guidance. Circulation 1999;100:2085–92.

33. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.

34. Melo J, Adragao P, Neves J, et al. Surgery for atrial fibrillation using radiofrequency catheter ablation: assessment of results at one year. Eur J Cardiothorac Surg 1999;15:851–4.

35. Gaita F, Riccardi R, Caponi D, et al. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease. Correlation of electroanatomic mapping and long-term clinical results. Circulation 2005;111: 145–51.

36. Karch MR, Zrenner B, Deisenhofer I, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation. A randomized comparison between 2 current ablation strategies. Circulation 2005;111:2875–80.

37. Sanders P, Berenfeld O, Hocini M, et al. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. Circulation 2005;112:789–97.

38. Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8-1/2-year clinical experience with surgery for atrial fibrillation. Ann Surg 1996;224:267–73.

39. Gaita F, Gallotti R, Calò L, et al. Limited posterior left atrial cryoablation in patients with chronic atrial fibrillation undergoing valvular heart surgery. J Am Coll Cardiol 2000;36:159–66.

40. Kumagai K, Uno K, Khrestian C, Waldo AL. Single site radiofrequency catheter ablation of atrial fibrillation: studies guided by simultaneous multisite mapping in the canine sterile pericarditis model. J Am Coll Cardiol 2000;36:917–33.

41. Oral H, Ozaydin M, Chugh A, et al. Role of the coronary sinus in maintenance of atrial fibrillation. J Cardiovasc Electrophysiol 2003;14: 1329–36.

42. Singh S, Johnson PI, Lee RE, et al. Topography of cardiac ganglia in the adult human heart. J Thorac Cardiovasc Surg 1996;112:943–53.

43. Schauerte P, Scherlag BJ, Pitha J, et al. Catheter ablation of cardiac autonomic nerves for prevention of vagal atrial fibrillation. Circulation 2000;102:2774–80.

44. Ouyang F, Antz M, Ernst S, et al. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins. Lessons from double lasso technique. Circulation 2005;111:136–44.