Long-Term Clinical Results of 2 Different Ablation Strategies in Patients With Paroxysmal and Persistent Atrial Fibrillation

Fiorenzo Gaita, MD; Domenico Caponi, MD; Marco Scaglione, MD; Antonio Montefusco, MD; Antonella Corleto, MD; Fernando Di Monte, PhD; Daniele Coin, PhD; Paolo Di Donna, MD; Carla Giustetto, MD

**Background**—Data regarding the long-term efficacy of atrial fibrillation (AF) ablation are still lacking.

**Methods and Results**—Two hundred four consecutive patients symptomatic for paroxysmal or persistent/permanent AF were randomly assigned to 2 different ablation schemes: pulmonary vein isolation (PVI) and PVI plus left linear lesions (LL). Primary end point was to assess the maintenance of sinus rhythm (SR) after procedures 1 and 2 in the absence of antiarrhythmic drugs in a long-term follow-up of at least 3 years.

**Paroxysmal AF**—With a single procedure at 12-month follow-up, 46% of patients treated with PVI maintained SR, whereas at 3-year follow-up, 29% were in SR; using the “PVI plus LL” at the 12-month follow-up, 57% of patients were in SR, whereas at the 3-year follow-up, 53% remained in SR. After a second procedure, the long-term overall success rate without antiarrhythmic drugs was 62% with PVI and 85% with PVI plus LL.

**Persistent/Permanent AF**—With a single procedure at the 12-month follow-up, 27% of patients treated with PVI were in SR, whereas at the 3-year follow-up, 19% maintained SR; using the PVI plus LL with a single procedure at the 12-month follow-up 45% of patients were in SR, whereas at the 3-year follow-up, 41% remained in SR. After a second procedure, the long-term overall success rate without antiarrhythmic drugs was 39% with PVI and 75% with PVI plus LL.

**Conclusions**—A long-term follow-up of AF ablation shows that short-term results cannot be considered permanent because AF recurrences are still present after the first year especially in patients who have had “PVI” strategy. PVI isolation plus LL is superior to the PVI strategy in maintaining SR without antiarrhythmic drugs after procedures 1 and 2 both in paroxysmal and persistent AF. (Circ Arrhythmia Electrophysiol. 2008;1:269-275.)

**Key Words:** ablation ■ arrhythmia ■ atrial fibrillation ■ catheter ablation ■ follow-up

Atrial fibrillation (AF) is the most frequent supraventricular arrhythmia. It is associated with increased morbidity and mortality but its management is still under debate. The limited success of drug treatment has stimulated an exploration of interventional treatment options. Therefore, in the past decade, various ablative procedures, both surgical and transcatheter, have been proposed.1–7 Most of the procedures aim at the isolation of the pulmonary veins to eliminate the initiating triggers of AF or at the creation of linear lesions (LL) to modify the substrate that perpetuates AF. However, it is difficult to judge the efficacy of the individual ablation strategy on the basis of clinical results. In fact, the available studies have shown variable percentages of success partly attributed to the variable percentage of types of AF, paroxysmal or persistent, presented in the patient population selected. Furthermore, different ablation schemes were used, varying procedural and clinical endpoints were considered, and the use of concomitant antiarrhythmic drugs (AADs) has not always been clarified.

**Editorial see p 238**

**Clinical Perspective see p 275**

Most importantly, little information is available as to the long-term clinical results. In fact, follow-ups reported were relatively short, often <1 year. In addition, it is not always possible to assess how many procedures have been necessary to achieve the success rates reported.

The aim of our study was to assess, in a prospective and randomized fashion, the maintenance of sinus rhythm (SR) in the absence of AADs in the long term, at least 3 years, using 2 different ablation strategies, pulmonary vein isolation (PVI) alone versus PVI plus LL, in 2 different groups of AF, paroxysmal and persistent, both after procedures 1 and 2. Moreover, these long-term results were compared with the 12-month results.

**Methods**

**Study Population**

Two hundred four consecutive patients who had radiofrequency catheter ablation for symptomatic, paroxysmal, or persistent/perma-
puncture or through a patent foramen ovale, when present. In case of
and recording. The left atrium (LA) was accessed by transseptal
electrode catheter was positioned in the coronary sinus for pacing
before the endorphin study, to visualize the esophagus. An octapolar
heparin was administered instead. An oral bolus of barium was given
discontinued 3 days before admission and low-molecular weight
warfarin for at least 1 month before the procedure. Warfarin was

to rule out the presence of atrial thrombi. Patients have been on
transesophageal echocardiography was performed in all the patients

electrophysiological study. Before the electrophysiological study, a

After written informed consent was obtained, patients underwent the

Catheter Ablation
Electrophysiological Study and Radiofrequency
Catheter Ablation

Electrophysiological Study and Radiofrequency
Catheter Ablation

After written informed consent was obtained, patients underwent the
electrophysiological study. Before the electrophysiological study, a
transesophageal echocardiography was performed in all the patients
to rule out the presence of atrial thrombi. Patients have been on
warfarin for at least 1 month before the procedure. Warfarin was
discontinued 3 days before admission and low-molecular weight
heparin was administered instead. An oral bolus of barium was given
before the endorphin study, to visualize the esophagus. An octapolar
electrode catheter was positioned in the coronary sinus for pacing
and recording. The left atrium (LA) was accessed by transseptal
puncture or through a patent foramen ovale, when present. In case of

Figure 1. A, Left atrium 3D reconstruction in patient who had pulmonary
vein isolation. B, Left anterior oblique (LAO) view showing multipolar catheter in left
superior pulmonary vein and ablation
catheter at the ostium of the same pul-
monary vein. C, Left atrium 3D recon-
struction in patient who had pulmonary
vein isolation plus linear lesions. D, LAO
view showing multipolar catheter in left
superior pulmonary vein and ablation

catheter at the ostium of the right inferior
pulmonary vein.

The primary end point was to assess the maintenance of SR in the
absence of AADs over a long-term follow-up, at least 3 years, using
2 different ablation strategies, PVI alone versus PVI plus LL, in 2
different groups of AF, paroxysmal and persistent, both after
procedures 1 and 2. Moreover, these long-term results were com-
pared with the 12-months results.

The primary end point was to assess the maintenance of SR in the
absence of AADs over a long-term follow-up, at least 3 years, using
2 different ablation strategies, PVI alone versus PVI plus LL, in 2
different groups of AF, paroxysmal and persistent, both after
procedures 1 and 2. Moreover, these long-term results were com-
pared with the 12-months results.

Electrophysiological Study and Radiofrequency
Catheter Ablation

After written informed consent was obtained, patients underwent the
electrophysiological study. Before the electrophysiological study, a
transesophageal echocardiography was performed in all the patients
to rule out the presence of atrial thrombi. Patients have been on
warfarin for at least 1 month before the procedure. Warfarin was
discontinued 3 days before admission and low-molecular weight
heparin was administered instead. An oral bolus of barium was given
before the endorphin study, to visualize the esophagus. An octapolar
electrode catheter was positioned in the coronary sinus for pacing
and recording. The left atrium (LA) was accessed by transseptal
puncture or through a patent foramen ovale, when present. In case of

absence of a patent foramen ovale, a guide wire was introduced into
the LA by a transseptal puncture using a 8F long sheath (Daig, St
Jude or Preface, Cordis-Webster). The sheath was perfused during
the procedure with heparinized NaCl 0.9% at 120 mL/h. A multipolar
catheter (Orbiter, Bard or Lasso, Biosense Webster) was inserted
through the long sheath to map the pulmonary vein ostia in both the
ablation procedures. All the procedures were performed using a
3.5-mm irrigated tip ablation catheter (Navistar, Biosense Webster)
advanced into the LA through the same hole whenever possible,
otherwise a second transseptal puncture was performed. The venous
sheath soon after was moved to the right atrium and continuously
perfused with heparinized 5% dextrose-water solution, or heparin-
ized 0.9% NaCl. A bolus of intravenous heparin was given bolus
(50U pro kg) to maintain an activated clotting time at least 200
seconds throughout the procedure. Deep sedation was achieved by
means of intravenous phentanyl, midazolam, and propofol.

A 3D reconstruction of the LA and PV ostia, using an electroana-
tomic mapping system (Carto, Biosense-Webster) was performed in
all patients and PV electric activity was assessed using a decapolar
ring catheter (Orbiter PV Bard and Lasso Biosense-Webster). The
aim of the ablation procedure was to obtain a complete electric
isolation of PVs in group A patients and a complete electric isolation
plus the creation of LL interconnecting the upper PV ostia (roof line)
and the left inferior PV, down to the mitral annulus, in group B
patients (Figure 1). RF was applied using an open irrigated tip
catheter (Navistar Thermocool, Biosense Webster) with power out-
put, up to 30 W, close to the PV ostia and up to 45 W while creating
the roof line and the left mitral isthmus line, using an irrigation rate
of 20 to 30 mL/min (0.9% saline infused with the Cool Flow Pump,
Biosense Webster) to maintain a tip temperature of <45°.

The PV isolation was carried out anatomically and confirmed
electrophysiologically. The 3D reconstructed anatomy guided the
encircling of the PVs, performed by ablating a wide area at 1 to 2 cm
from their ostia with the aim of eliminating all the atrial potentials,
or their abatement <0.05 mV. If a complete pulmonary vein electric
disconnection was not present after the anatomic encircling a
segmental ablation of the pulmonary vein was carried out. PVI was
defined by complete elimination, or dissociation of PV potentials, determined by the circular mapping catheter, positioned at the PV ostia.

The lines were performed with an anatomic approach, using a CARTO map. This map allowed us to guide the catheter along the predetermined lines on the LA roof and the left isthmus, making it also possible to return to points previously ablated. Moreover, the CARTO map allowed for the identification of the disappearance of the atrial potentials, or their reduction <0.05 mV. The creation of an effective mitral isthmus linear lesion was assessed by mapping the activation detour during pacing from both sides of the lesion, as previously described5 and assessing the CARTO activation map postablation. If a complete block was not achieved, epicardial ablation within the coronary sinus was not considered because of the risk of complications, but adjacent lines were added to slow conduction to an interval of the local double potential >80 ms. The conduction block along the roof was assessed demonstrating a corridor of double potentials along the entire length of the roof during pacing from the distal coronary sinus by point-by-point mapping.

Finally, all patients had radiofrequency ablation of the cavo-tricuspid isthmus.

Follow-Up
During hospitalization, the ECG was continuously monitored and standard heparin infusion maintained for 24 hours after the procedure. Low-molecular weight heparin and warfarin therapy were instituted on the following day; heparin was stopped when international normalized ratio was in the therapeutic range of 2 to 3. Patients were discharged with antiarrhythmic therapy that was discontinued after 2 months (blanking period). After hospital discharge, patients were followed with clinical examination and ECG and an event recorder was applied. Recurrence was defined as an episode of palpitations lasting >30 seconds or AF, or atrial flutter episodes >30 seconds documented by Holter monitoring, 12-lead ECG or event recorder. All the recurrences were considered failures. A repeat ablation procedure was recommended for recurrences after the blanking period. The second procedure was performed within 2 months depending on the availability of the electrophysiology laboratory. An assessment of the completeness of the lines and the electric isolation of the pulmonary veins was carried out during the second procedure. If conduction gaps were present, or if the pulmonary veins were not isolated, ablation was performed according to the ablation scheme used during the first procedure.

Long-term success was defined as the maintenance of SR without AAD therapy after procedures 1 or 2 during the follow-up excluding the first 2 months (blanking period).

Statistical Methods
The randomization process was built as follows: a random X was extracted from a uniform distribution for any new patient. If X was <0.34, the patient was assigned to PVI ablation scheme, to PVI plus left LL otherwise. The patients were kept blind to the treatment received. Quantitative data were expressed as a mean±SD. Statistical analysis was performed using R software (2.4.1). The probability of survival free from recurrence was assessed using the Kaplan-Meier product-limit estimates. Kaplan-Meier estimates were compared using the long-rank test. The tests performed were 2-sided and statistical significance level was set at 0.05.

Statement of Responsibility
The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table. Clinical Characteristics of the Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>PVI (n=67)</th>
<th>PVI Plus LL (n=137)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.3 ± 9.0</td>
<td>56.0 ± 9.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Males</td>
<td>55 (82)</td>
<td>107 (78)</td>
<td>0.63</td>
</tr>
<tr>
<td>Time since AF onset, years</td>
<td>5.7 ± 4.5</td>
<td>4.9 ± 3.8</td>
<td>0.16</td>
</tr>
<tr>
<td>Paroxysmal AF/persistent</td>
<td>41 (61)</td>
<td>84 (61)</td>
<td>1.00</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>8 (12)</td>
<td>21 (15)</td>
<td>0.66</td>
</tr>
<tr>
<td>Left atrial diameter, mm</td>
<td>42 ± 7</td>
<td>44 ± 6</td>
<td>0.17</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>48 ± 7</td>
<td>49 ± 7</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%).

Results

Early Results
We analyzed a series of 204 consecutive patients (162 males; median age 55 years), 125 patients with paroxysmal AF and 79 patients with persistent/permanent AF. The patients had 5.2±4.0 years history of symptomatic AF; structural heart disease was present in 14%. The clinical baseline characteristics of the patients are depicted in the Table.

No significant differences in terms of mean age, mean duration of AF, or structural heart disease were present in the PVI group and the PVI plus linear lesion group. Mean LA ablation procedure time was 79.0±16.7 minutes for group A and 94.6±17.5 minutes for group B (P <0.001), without a significant difference in fluoroscopy time (40.4±13.5 versus 44.2±15.9 minutes, P >0.05). Complete PV isolation was acutely achieved in all patients. Complete mitral isthmus block was obtained in 42 of 137 (31%) of the “PVI plus LL” strategy patients; in the remaining 95 (69%) patients, acute conduction slowing along the mitral isthmus during coronary sinus pacing was observed, with a mean atrial electrogram interval of 120±18 ms. Conduction block along the roof was achieved in 92% of the patients. Cavo-tricuspid isthmus ablation was successful in 100% of patients.

Mid–Long-Term Outcome

Paroxysmal AF

PVI Strategy
Considering only 1 procedure at the 12-month follow-up, 19 of 41 patients (46%) were in SR without AAD. Among the 22 patients with recurrences at 1-year follow-up, 4 (18%) patients were asymptomatic. At the end of follow-up of 41.4±6.2 months, only 12 (29%) patients remained in SR (Figure 2). Among the 29 patients with recurrences at the end of follow-up, 6 (21%) patients were asymptomatic. Therefore, the relative risk of recurrence within 12 months was estimated at 54% and 37% after 12 months. Twenty-nine of 41 (71%) patients experienced arrhythmia recurrence and a second procedure was proposed. It was performed in 27 patients because 2 patients declined the procedure because of the maintenance of SR while taking previously ineffective AADs and because of a significant clinical improvement. AF
recurrence was the reason of a redo procedure in 22 patients, atypical atrial flutter in 3 patients, and typical atrial flutter in 2 patients. All the 5 patients with typical and atypical atrial flutter underwent successful ablation. In the 3 patients with atypical atrial flutter, a reentry circuit involving the left inferior PV was found in 1 case, whereas in the remaining 2 patients a microreentry involving the right superior PV was the mechanism. Among the remaining 22 patients with AF recurrence a recovery of veno-atrial conduction in at least 1 or more PVs was found in all the patients. A complete PV isolation was achieved with the second procedure. With the addition of a second procedure, excluding the 2 patients who refused the second ablation, the overall success rate without AAD at the end of follow-up was 62% (24 of 39 patients; Figure 3).

**PVI Plus LL**

Considering only 1 procedure at the 12-month follow-up, 48 of 84 patients (57%) were in SR without AAD. Among the 36 patients with recurrences at 1-year follow-up, 7 (19%) patients were asymptomatic. At the end of the follow-up of 39.7±5.5 months, 45 of 84 patients (53%) remained in SR (Figure 2). Among the 39 patients with recurrences at the end of follow-up, 8 (21%) patients were asymptomatic. Therefore, the relative risk of AF recurrence within 12 months is 43% and after 12 months was estimated at 6%. Thirty-nine of 84 (46%) patients experienced arrhythmia recurrence and a second procedure was proposed. It was performed in 29 patients because 10 patients declined the procedure. Repeat ablation was performed for recurrent AF in 24 patients, and for atypical atrial flutter in 5 patients. The mechanism of the atypical atrial flutter was a conduction gap in the lesion line of the left isthmus in 3 cases, a conduction gap in the roof line in 1 patient, and a macroreentry circuit in the lateral wall of the right atrium in the last patient. Among the 24 patients with AF recurrence, a recovery of veno-atrial conduction in at least one or more PVs was found in all the patients. A complete PV isolation was achieved with the second procedure. Ablation for atypical atrial flutter using entrainment technique and the 3D electroanatomic mapping was performed in all the 5 patients with long-term success. With the addition of a second procedure, excluding the 10 patients who refused the redo ablation, the overall success rate without AAD at the end of follow-up was 85% (63 of 74 patients; Figure 3).

**Figure 2.** Kaplan-Meier curves of maintenance of sinus rhythm in long term after the first procedure in patients with paroxysmal atrial fibrillation (left) and persistent/permanent atrial fibrillation (right).

**Figure 3.** Kaplan-Meier curves of maintenance of sinus rhythm after the second procedure in patients with paroxysmal and persistent/permanent AF.
Persistent/Permanent AF

PVI Strategy
Considering only one procedure at the 12-month follow-up, 7 of 26 patients (27%) were in SR without AAD. Among the 19 patients with recurrences, 3 (16%) were asymptomatic at 1-year follow-up. At the end of follow-up, only 5 of 26 patients (19%) remained in SR (Figure 2). Among the 21 patients with recurrences, 4 (19%) were asymptomatic at the end of follow-up. Therefore, the relative risk of recurrence within 12 months was estimated at 73% and 29% after 12 months. Twenty-six of 26 patients (81%) experienced arrhythmia recurrence and a second procedure was proposed. It was performed in 18 patients because 3 patients declined the procedure. AF recurrence was the reason of a redo procedure in 17 patients, atypical atrial flutter in 1 patient. Among the 17 patients with AF, a recovery of veno-atrial conduction in at least one or more PVs was found in all the patients. A complete PV isolation was achieved with the second procedure. In the only patient with atypical atrial flutter, the 3D electroanatomic mapping and the entrainment technique confirmed that the mechanism was a reentry circuit around the left PVs. RF ablation was successful in the long term. With the addition of a second procedure, excluding the 3 patients who refused a repeat ablation, the overall success rate of AAD at the end of follow-up was 39% (9 of 23 patients; Figure 3).

PVI Plus LL
Considering only 1 procedure at the 12-month follow-up, 24 of 53 patients (45%) were in SR without AAD. Among the 29 patients with recurrences, at 1-year follow-up 5 (17%) were asymptomatic. At the end of the follow-up, 22 of 53 (41%) remained in SR (Figure 2). Among the 31 patients with recurrences, 6 (19%) were asymptomatic at the end of follow-up. Therefore, the relative risk of AF recurrence within 12 months is 55% and after 12 months was estimated at 8%. Thirty-one of 53 patients (58%) experienced arrhythmia recurrence and a second procedure was proposed. It was performed in 25 patients because 6 patients declined the procedure. Repeat ablation procedures were performed for recurrent AF in 16 patients, atypical atrial flutter in 8 patients, and typical atrial flutter in 1 patient. Among the 16 patients with AF recurrence, all had recovery of conduction to one or more PV; and PV isolation was achieved with the second procedure. Typical atrial flutter was successfully ablated. Among the 8 patients with atypical atrial flutter, ablation was successful in 7 patients. The mechanism of atypical atrial flutter was a conduction gap in the left isthmus in 3 cases, and a microreentry involving the left inferior PV, the RIPV, the posterior wall of the LA in 3 cases, respectively, and a macroreentry involving the vena cava in the last patient. In the patient in whom the ablation was unsuccessful, it was not possible to define a specific reentry circuit sustaining the arrhythmia.

Therefore with the addition of a second procedure, excluding the 6 patients who refused a repeat ablation, the overall success rate without AAD at the end of follow-up was 75% (35 of 47 patients; Figure 3).

Comparison of the Results on the Basis of the Ablation Strategy and the Type of AF
The PVI plus LL strategy showed to be statistically significantly more effective than the “PVI alone” strategy in patients with persistent/permanent AF both at short- (12 months) and long-term (36 months) follow-up. On the other end considering patients with paroxysmal AF at the 12-month follow-up, the 2 strategies did not show a statistically significant difference, whereas the difference became significant in a long-term follow-up. These behavior is correlated to the higher number of AF recurrences in the “PVI” group also beyond the first year of follow-up. Atrial flutter was more frequent in the group of PVI plus linear lesion than in PVI alone group without reaching the statistical significance (9% versus 6%, P = 0.559). Comparing the results according to the type of AF, it emerges that ablation is significantly more effective either at short term and long term in patients with paroxysmal rather than persistent/permanent AF regardless of the ablation strategy (Figure 4).

Complications
No procedure-related death was observed. Cardiac tamponade occurred in 2 patients who recovered successfully after immediate pericardiocentesis. Transient ischemic attacks occurred in 2 patients without neurological sequelae. An arterio-venous fistula requiring surgery occurred in 1 patient. In one case, esophageal ulceration was visualized at the esophagastroduodenoscopy, which recovered uneventfully. No statistically significant difference in the complication rate was present among the 2 groups. One patient died of sudden death after 12 months from the procedure; at the time of death, the patient was in SR.

Discussion
The main findings of the study are the following:

a. Success rate at the 12-month follow-up cannot be considered a permanent success.

b. About 50% of patients undergoing AF ablation requires a second procedure.

c. The efficacy of AF ablation in a long term is higher in patients with paroxysmal AF compared with patients with persistent AF regardless of the ablation strategy (PVI or PVI plus LL).
d. PVI plus LL strategy is more effective in maintaining SR of AAD. In patients with paroxysmal AF, the difference between the PVI plus LL and the PVI alone strategy is not statistically significant at 12 months, whereas the difference becomes statistically significant in the long-term follow-up because of the higher number of recurrences in the PVI group. In patients with persistent/permanent, the PVI plus LL strategy is more effective at 12 months and the better results persist over the long-term follow-up.

The results of our study show the importance to assess the clinical results with a long-term follow-up. In fact, in our series, the percentage of AF recurrences is very high in the first 12 months, but it is significant also in the following period between 12 and 36 months making necessary a second procedure in a significant proportion of patients: about 75% in the PVI strategy population and about 45% in PVI plus LL strategy population. This finding can be explained by the fact that the longer the follow-up, the higher is the possibility that recovery of veno-atrial conduction and perturbations in vagal and adrenergic innervation of the atrium may become relevant to the recurrence of AF. In addition, the process of atrial fibrosis leading to increased and inhomogeneous dispersion of conduction abnormalities including block, slow conduction, and uncoupling of muscle bundle may favor the initiation and perpetuation of AF. The analysis of our data reveals that in all the patients with AF recurrences, a recovery of venoatrial conduction was present. On the basis of this evidence, short-term follow-up results cannot be inferred as permanent. This observation has important clinical consequences especially as far as the anticoagulation therapy is concerned. It is prudent and reasonable, therefore, not to discontinue the anticoagulation therapy in patients at risk for thromboembolic complications who had ablation even if that was the principal reason of the procedure.

Furthermore, the different ablation results in patients with paroxysmal AF and persistent AF are not surprising, because the mechanism of the AF is thought to be different. In fact, paroxysmal AF is mainly focally induced and the PVs have been considered as the predominant trigger locations for AF initiation. Consequently, they have become the main target of the ablation strategy population. This finding can be explained by the fact that the longer the follow-up, the higher is the possibility that recovery of veno-atrial conduction and perturbations in vagal and adrenergic innervation of the atrium may become relevant to the recurrence of AF. In addition, the process of atrial fibrosis leading to increased and inhomogeneous dispersion of conduction abnormalities including block, slow conduction, and uncoupling of muscle bundle may favor the initiation and perpetuation of AF. The analysis of our data reveals that in all the patients with AF recurrences, a recovery of venoatrial conduction was present. On the basis of this evidence, short-term follow-up results cannot be inferred as permanent. This observation has important clinical consequences especially as far as the anticoagulation therapy is concerned. It is prudent and reasonable, therefore, not to discontinue the anticoagulation therapy in patients at risk for thromboembolic complications who had ablation even if that was the principal reason of the procedure.

The results of our study show the importance to assess the clinical results with a long-term follow-up. In fact, in our series, the percentage of AF recurrences is very high in the first 12 months, but it is significant also in the following period between 12 and 36 months making necessary a second procedure in a significant proportion of patients: about 75% in the PVI strategy population and about 45% in PVI plus LL strategy population. This finding can be explained by the fact that the longer the follow-up, the higher is the possibility that recovery of veno-atrial conduction and perturbations in vagal and adrenergic innervation of the atrium may become relevant to the recurrence of AF. In addition, the process of atrial fibrosis leading to increased and inhomogeneous dispersion of conduction abnormalities including block, slow conduction, and uncoupling of muscle bundle may favor the initiation and perpetuation of AF. The analysis of our data reveals that in all the patients with AF recurrences, a recovery of venoatrial conduction was present. On the basis of this evidence, short-term follow-up results cannot be inferred as permanent. This observation has important clinical consequences especially as far as the anticoagulation therapy is concerned. It is prudent and reasonable, therefore, not to discontinue the anticoagulation therapy in patients at risk for thromboembolic complications who had ablation even if that was the principal reason of the procedure.

Furthermore, the different ablation results in patients with paroxysmal AF and persistent AF are not surprising, because the mechanism of the AF is thought to be different. In fact, paroxysmal AF is mainly focally induced and the PVs have been considered as the predominant trigger locations for AF initiation. Consequently, they have become the main target for the interventional treatment of paroxysmal AF with satisfactory results. On the other end, persistent AF is more substrate dependent and the modifications of larger areas of atrial tissue may be needed to modify the arrhythmogenic substrate to prevent AF recurrence and this explains why in patients with persistent/permanent AF, the results are better with the addition of LL. This fact has been already seen by previous studies assessing transcatheter ablation and surgical ablation in patients with permanent AF. In the latter study, the PVI alone strategy showed only 25% of success rates, whereas the PVI plus linear lesion approach was much more effective especially if complete lines were demonstrated (86%). On the other end, the better outcome with the addition of linear lines in patients with paroxysmal AF confirmed the clinical results in the short-term follow-up as previously reported.

Besides the higher efficacy, another advantage of the PVI plus LL approach is the fact that with this strategy the necessity of a second procedure was reduced and more importantly the PVI plus LL strategy determines a lower percentage of recurrences especially after the first year.

These results are in line with the different pathogenesis of AF. Adding LL implies a greater amount of ablated atrial tissue creating a compartmentalization of the LA and reducing the critical mass necessary to sustain AF. Furthermore, LL can isolate the mother rotor zone or modify the electroanatomical substrate targeting areas of complex fractionated activity. In addition, PVs isolation alone does not address AF arising from non-PV.

Nonetheless, LA linear ablation still remains technically challenging and it is often difficult to obtain the complete block of the entire LL. The remaining conduction gaps can favor the occurrence of the atypical flutters that varies from 2.6% to 31%. In our series, in patients who had PVI plus LL, the incidence of postablation atrial flutters was higher in the follow-up. Anyway, mapping either with the electroanatomical 3D reconstruction or with the entrainment technique, it has been possible to define the reentry circuit in most patients and ablate it.

Limitations
The follow-up in our study has been performed according to the actual clinical practice so that a limitation is the fact that extended electrocardiographic monitoring was not used. It is conceivable, therefore, that asymptomatic episodes of AF occurring outside the monitoring periods were missed. As a consequence, asymptomatic episodes documented in the long term may have already been present and recurrences first recognized beyond the first year may be simply because of the delayed diagnosis.

Another limitation is represented by the fact that few patients refused to have a second procedure because they improved clinically with the addition of AADs previously ineffective. These patients have been calculated as failures after the first procedure, but they have not been included in the assessment of the efficacy after the second procedure because the second procedure has not been performed and the outcome would not have been foreseen. Therefore, reporting overall clinical efficacy after the second procedure excluding the patients who refused to have repeat ablation may create a bias for a more favorable outcome.

Conclusions
Although various ablative strategies for AF have been designed during the last 10 years, the efficacy without AAD in patients with paroxysmal and persistent AF in the long term is still unclear.

Short-term follow-up results cannot be considered permanent because AF recurrences are still present after the first year. This is more evident in patients who have had PVI strategy alone. In a large percentage of the patients, a second procedure is required.

AF ablation is more effective in patients with paroxysmal AF compared with patients with persistent AF regardless of the ablation strategy (PVI or PVI plus LL).

PVI plus LL strategy is more effective in maintaining SR without AAD. The difference between PVI plus LL and PVI alone strategy is not statistically significant at 12 months in
Atrial fibrillation is a common arrhythmia associated with increased morbidity and mortality. Pharmacological therapy to maintain sinus rhythm has been disappointing. Catheter ablation has been recently developed, and most studies report efficacy after relatively short-term follow-up of generally 1 year. The durability of short-term results has not been demonstrated and may not be equivalent to long-term results. To our knowledge, our study is the first prospective randomized study that evaluates the short-term (1 year) and long-term (3 years) efficacy of 2 common ablation strategies, pulmonary vein isolation and pulmonary vein isolation plus linear lesions in the left atrium, for patients with paroxysmal atrial fibrillation and patients with persistent atrial fibrillation. We show that regardless of ablation strategy, short-term efficacy cannot be considered permanent; arrhythmia recurrences are still possible during longer follow-up, especially when the pulmonary vein isolation strategy is used. This fact raises concern about the risk of discontinuing antiocoagulation after short-term success in patients who have risk factors for thromboembolism. We also show that regardless of ablation strategy, efficacy is better for patients with paroxysmal rather than persistent atrial fibrillation. These findings suggest that use of ablation in patients with paroxysmal atrial fibrillation before the progression to the persistent form may improve long-term outcome.

**CLINICAL PERSPECTIVE**

Atrial fibrillation is a common arrhythmia associated with increased morbidity and mortality. Pharmacological therapy to maintain sinus rhythm has been disappointing. Catheter ablation has been recently developed, and most studies report efficacy after relatively short-term follow-up of generally <1 year. The durability of short-term results has not been demonstrated and may not be equivalent to long-term results. To our knowledge, our study is the first prospective randomized study that evaluates the short-term (1 year) and long-term (3 years) efficacy of 2 common ablation strategies, pulmonary vein isolation and pulmonary vein isolation plus linear lesions in the left atrium, for patients with paroxysmal atrial fibrillation and patients with persistent atrial fibrillation. We show that regardless of ablation strategy, short-term efficacy cannot be considered permanent; arrhythmia recurrences are still possible during longer follow-up, especially when the pulmonary vein isolation strategy is used. This fact raises concern about the risk of discontinuing anticoagulation after short-term success in patients who have risk factors for thromboemboli. We also show that regardless of ablation strategy, efficacy is better for patients with paroxysmal rather than persistent atrial fibrillation. These findings suggest that use of ablation in patients with paroxysmal atrial fibrillation before the progression to the persistent form may improve long-term outcome.
Long-Term Clinical Results of 2 Different Ablation Strategies in Patients With Paroxysmal and Persistent Atrial Fibrillation
Fiorenzo Gaita, Domenico Caponi, Marco Scaglione, Antonio Montefusco, Antonella Corleto, Fernando Di Monte, Daniele Coin, Paolo Di Donna and Carla Giustetto

Circ Arrhythm Electrophysiol. 2008;1:269-275
doi: 10.1161/CIRCEP.108.774885

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/1/4/269

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org//subscriptions/