Arrhythmia/Electrophysiology

Left Atrial Appendage
An Underrecognized Trigger Site of Atrial Fibrillation

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Background—Together with pulmonary veins, many extrapulmonary vein areas may be the source of initiation and maintenance of atrial fibrillation. The left atrial appendage (LAA) is an underestimated site of initiation of atrial fibrillation. Here, we report the prevalence of triggers from the LAA and the best strategy for successful ablation.

Methods and Results—Nine hundred eighty-seven consecutive patients (29% paroxysmal, 71% nonparoxysmal) undergoing redo catheter ablation for atrial fibrillation were enrolled. Two hundred sixty-six patients (27%) showed firing from the LAA and became the study population. In 86 of 987 patients (8.7%; 5 paroxysmal, 81 nonparoxysmal), the LAA was found to be the only source of arrhythmia with no pulmonary veins or other extrapulmonary vein site reconnection. Ablation was performed either with focal lesion (n=56; group 2) or to achieve LAA isolation by placement of the circular catheter at the ostium of the LAA guided by intracardiac echocardiography (167 patients; group 3). In the remaining patients, LAA firing was not ablated (n=43; group 1). At the 12±3-month follow-up, 32 patients (74%) in group 1 had recurrence compared with 38 (68%) in group 2 and 25 (15%) in group 3 (P<0.001).

Conclusions—The LAA appears to be responsible for arrhythmias in 27% of patients presenting for repeat procedures. Isolation of the LAA could achieve freedom from atrial fibrillation in patients presenting for a repeat procedure when arrhythmias initiating from this structure are demonstrated. (Circulation. 2010;122:109-118.)

Key Words: atrial appendage ■ atrial fibrillation ■ catheter ablation

Catheter ablation has been shown to be an effective therapy for the treatment of drug-refractory atrial fibrillation (AF).1-3 In 1998, Haııssaguerre and colleagues4 described firing originating from the pulmonary veins (PVs) as an important source initiating AF. PVs have become the most important target for catheter ablation of AF, although controversy still exists as to the extent of ablation that should be performed outside of the PVs, particularly in nonparoxysmal AF.5,6

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For those reasons and to increase the procedural success rate, several studies have shown that together with the PVs, many extra-PV areas may be the source of initiation and maintenance of AF.7-14 The most common sites are the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, and left atrial (LA) posterior wall. The LA appendage (LAA) is an underreported site of initiation of AF.15 Here, we aim to report on the prevalence of firing from the LAA and the optimal strategy to eliminate these triggers to increase the procedural success rate.

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Heart Association/American College of Cardiology.²,³ Of the 987 consecutive patients (29% paroxysmal AF; PER, persistent AF; and LSP, long-standing persistent AF), 845 underwent their first ablation procedure. The institutional ethics committees approved the study. All patients signed an informed written consent before the procedure. The primary end point of this study was freedom from AF/ATs for at least 1 year after the procedure. The secondary end point was freedom from AF/ATs for at least 2 years after the procedure. The primary end point was defined as the absence of all ATs or AF for at least 1 year. The secondary end point was defined as the absence of all ATs or AF for at least 2 years.

Methods

Nine hundred eighty-seven consecutive patients (29% paroxysmal and 71% nonparoxysmal) undergoing repeat catheter ablation for symptomatic and drug-resistant AF were screened for this study. Patients were enrolled at the Texas Cardiac Arrhythmia Institute, Austin, Tex; California Pacific Medical Center, San Francisco; Catholic University, Rome, Italy; Metro-Health Hospital, Case Western University, Cleveland, Ohio; Akron General Hospital, Akron, Ohio; Stanford University, Palo Alto, Calif; and Ospedale dell’Angelo, Mestre, Venice, Italy.

The definitions of paroxysmal, persistent, and long-standing persistent AF followed the consensus documents by the Heart Rhythm Society/European Heart Rhythm Association/American Heart Association/American College of Cardiology.²,³ Of the 987 patients undergoing repeat procedures, we included only the patients who showed LAA firing at baseline or after administration of isoproterenol. Of the 987 patients undergoing repeat ablation, 721 did not show LAA firing and were not included in the analysis. The remaining 266 patients met the inclusion criteria and constituted the study population.

LAA firing was defined as consistent premature atrial contractions (PACs) with the earliest activation in the LAA (at least 10 in 1 minute) or as AF/atrial tachycardia (AT) originating from the LAA. At each participating center, the physician performing the procedure could choose from among the following 3 strategies: ignore the LAA firing and perform a standard procedure (group 1), perform focal ablation of the LAA (group 2), or perform LAA electric isolation (group 3; Figure 1). In all groups, if AT/AF persisted at the end of the procedure, cardioversion was used to restore sinus rhythm.

All patients signed an informed written consent before the procedure. The institutional ethics committees approved the study.

Standard Ablation Procedure

Electrophysiological Study

Two right groin accesses were used for transseptal catheterization. Transseptal access was obtained via 2 separate puncture sites. A 20-mm, decapolar circular mapping catheter was used for mapping (Lasso, Biosense-Webster, Baldwin Park, Calif), and a 3.5-mm open irrigated-tip ablation catheter ( Biosense-Webster) was used for ablation. An 11F left femoral venous access was used to guide a 10F phased-array ultrasound imaging catheter (Acunav, Acuson, Mountain View, Calif) in the right atrium.⁵,⁶,¹⁶,¹⁷ The right internal jugular vein was accessed and used to place a 20-pole catheter; the distal poles were positioned in the coronary sinus, and the proximal poles were placed along the crista terminalis.

Before transseptal access, all patients received a heparin bolus of 100 to 150 U/kg and then an infusion of 1000 U/h adjusted to maintain an activated coagulation time >350 seconds. Antiarrhythmic drugs (AADs) were discontinued 5 days before the ablation. Patients on amiodarone discontinued the medication 5 to 6 months before the procedure.

Briefly, PV antrum isolation was performed, guided by a circular mapping catheter and by intracardiac echocardiography, along with empirical isolation of the superior vena cava.⁵,⁶,¹⁶,¹⁷ In patients with paroxysmal AF, the PV antra and the portion of the posterior wall contained within the PV area were targeted during the procedures with exit block as the end point.⁵ In patients with persistent and long-standing persistent AF, the electric isolation of the PVs was extended to the entire posterior wall down to the coronary sinus and to the left side of the septum.⁵,¹⁶

Ablation of the LAA

At the beginning of the procedures, in all patients, sites of reconnection around the PV antrum, posterior wall, and LA septum were checked and, when found, targeted with radiofrequency application with the above-mentioned technique. If patients were in atypical atrial flutter/tachycardia, this was mapped and ablated. Then, the ablation was extended to the LAA when triggers from this structure were documented in sinus rhythm before or after isoproterenol administration up to 30 μg/min. Ablation was performed by targeting the earliest electric activation of the PACs or AF/tachycardia (focal ablation; n = 56; group 2; Figure 2) or achieving LAA isolation guided by the activation on the circular catheter placed at the ostium of the LAA on the basis of intracardiac echocardiography (electric isolation; n = 167; group 3; Figures 3 through 5). If the operator decided not to ablate the LAA, the presence of LAA firing was documented in the database (group 1). The radiofrequency generator settings during LAA ablation included power up to 40 W while maintaining a catheter tip temperature of <41°C for a maximum of 20 seconds per ablation site.

End Points

The primary end point of this study was freedom from AF/ATs defined as no episodes of AF/AT without AADs lasting >32 seconds at follow-up. Episodes that occurred during the first 2 months (blanking period) after the procedure were not considered recurrences. AADs were discontinued in all patients 2 months after the ablation when no recurrences were present. In cases of recurrences, patients were given their previously ineffective AADs. Patients with arrhyth-
Figure 2. A, LA tachycardia initiation during isoproterenol infusion (30 μg/min) with the earliest activation at the level of the LAA (arrow). The circular catheter is positioned at the ostium of the LAA. B, Tachycardia termination during focal ablation (group 2). From top to bottom: surface ECG leads I, II, aVF, and V₃₃; right atrium crista (RA) from proximal (9 to 10) to distal (1 to 2); coronary sinus catheter (CS) from proximal (9 to 10) to distal (1 to 2); ablation catheter (ABL) from proximal (p) to distal (d); and circular catheter (L) from (1–2) to (9–10).
mia recurrence 3 months after the second procedure while on AADs were offered a repeat ablation.

Postablation Management and Follow-Up
All patients were discharged on warfarin with a target international normalized ratio of 2 to 3 and on previously ineffective AADs except for amiodarone. Warfarin was continued for a minimum of 6 months after the ablation procedure. All patients were followed up until the end of the study.

Patients were seen in the outpatient clinic at 3 months after the procedure and every 3 months thereafter. A 48-hour or 7-day Holter monitor was obtained at 3, 6, 9, 12, and 15 months after ablation. All patients were given an event recorder for 5 months and were asked to transmit recordings 4 times a week even when asymptomatic and anytime they experienced symptoms.

Figure 3. A, LAA isolation during sinus rhythm while the circular catheter is at the level of the LAA ostium. B, The first lesion at the earliest site resulted in modification of the activation sequence. C, A second lesion at the new earliest location achieved LAA isolation (arrow). From top to bottom: surface ECG leads I, II, and aVF; right atrium crista (RA) from proximal (9 to 10) to distal (1 to 2); coronary sinus catheter (CS) from proximal (9 to 10) to distal (1 to 2); ablation catheter (ABL) from proximal (p) to distal (d); and circular catheter (L) from (1–2) to (9–10).
In patients without recurrences, transthoracic (TTE) and transesophageal (TEE) echocardiographies were performed at 3 and 6 months to assess the E/A ratio, LAA flow velocity, and LAA contractility. Patients with poor LAA velocity (<0.3 m/s) were maintained on warfarin.

**Statistical Analysis**

Data are given as mean±SD if continuous and as counts and percent if categorical. Student *t* test, 1-way ANOVA, *χ²* test, and Fisher exact test were used to compare differences across groups. When required, posthoc analysis was performed with the Tukey-Kramer multiple-comparison method. Multivariable Cox regression was used to identify significant predictors of AF recurrence. All potential confounders were entered into the model on the basis of known clinical relevance or significant association observed in univariate analysis.

Controlling variables used in the model were age, gender, hyper-tension, diabetes mellitus, CHADS2 score, body mass index, and LAA isolation type (circumferential/segmental isolation versus focal ablation). Tests were run to examine the presence of multicollinearity of the covariates. The discrimination ability of the models in predicting AF recurrence was assessed by c statistics and receiver-operating characteristic curve. The proportional-hazard assumption for the covariates was tested by Schoenfeld residual analysis. This test did not have enough evidence to reject the proportionality. It was concluded that the data have satisfied the proportional-hazard assumption for this model. The hazard ratio (HR) and 95% confidence interval (CI) of AF recurrence were computed and are presented in table format. All tests were 2 sided, and a value of *P*<0.05 was considered statistically significant. Analyses were performed with SAS 9.2 (SAS Institute, Inc, Cary, NC).

**Results**

Among the 987 consecutive patients undergoing redo ablation during the study period, the prevalence of LAA PACs or AF/tachycardia with standard LA sites reconnection was 27% (266 patients). In 86 of 987 patients (8.7%; 5 paroxysmal, 81 nonparoxysmal), LAA was found to be the only source of arrhythmia (Table 1).

**Patient Characteristics**

There were 43 patients in group 1, 56 patients in group 2, and 167 patients in group 3. The 3 groups were comparable in baseline characteristics except that group 3 was significantly older and had a higher incidence of long-lasting persistent AF. In group 3, isolation was achieved with segmental lesions in 117 patients (70%) and with circumferential ablation in 50
patients (30%). The baseline characteristics are compared in Table 1.

Procedural Results
Of the 266 patients showing LAA firing, 165 patients (62%) entered the electrophysiology laboratory in AF/AT, and 48 (18%) entered the laboratory with consistent PACs. In the remaining 53 patients, PACs from the LAA were observed after challenge with isoproterenol in 38 patients (72%), whereas in 15 patients (28%), AF/ATs were initiated. In the subgroup of 86 patients in whom LAA was the only source of arrhythmia, 55 (64%) entered the electrophysiology laboratory in AF/AT and 17 (20%) with consistent PACs. In the remaining 14 patients, 11 patients (79%) showed PACs from the LAA after challenge with isoproterenol, whereas in 3 patients (21%), ATs were initiated. Persistence of AF/AT at end of the procedure was observed in 5 patients (12%) in group 1, 8 patients (14%) in group 2, and 17 patients (10%) in group 3. Sinus rhythm was achieved in these patients by cardioversion. The mean radiofrequency times for LAA isolation were 31 ± 6 while it was 15 ± 5 minutes for focal ablation (P < 0.001).

AF Recurrence After the First Redo Procedure
At the 12 ± 3-month follow-up, a total of 95 patients (36%) experienced AF recurrence after the redo procedure. In group 1, 32 patients (74%) had recurrence compared with 38 patients (68%) in group 2 and 25 patients (15%) in group 3. Distribution of recurrence by AF type is displayed in Table 2. Recurrence rates across the groups were compared through Tukey-Kramer multiple-comparison technique. The Tukey multiple-comparison results (Table I of the online-only Data Supplement) showed that group 3 had the lowest recurrence compared with the other 2 groups. Groups 1 and 2 did not have any significant difference in recurrence rates. Kaplan–Meier survival curves showing each group’s cumulative probability of AF-free survival are presented in Figure 6. The log-rank test of equality across groups for AF recurrence had a value of P < 0.001, showing a significant difference among the groups. Of the 86 patients in whom LAA was the only source of arrhythmic trigger, 21 underwent focal ablation, and 65 had circumferential isolation.

AF Recurrence After the Second Redo Procedure
In group 1, of the 32 patients (74%) who had recurrences at follow-up, 25 accepted a repeat procedure and underwent
LAA isolation. All 63 patients who had recurrence in groups 2 and 3 underwent LAA reisolation. In these 88 patients, the LAA was the only source of arrhythmia. In all patients, LAA isolation guided by circumferential mapping was performed.

At the end of the follow-up period, 6 patients experienced recurrences, and 82 (93%) were AT/AF free. Of interest, 3 of these 6 patients belonged to group 1. The Kaplan–Meier survival curve showing recurrence-free survival estimate is presented in Figure 6.

Univariate Analysis

Univariate Cox regression was performed to assess the prognostic role of baseline characteristics on AF recurrence. Type of AF, history of diabetes mellitus, and CHADS2 score showed independent associations with AF recurrence. The results of this analysis are presented in Table II of the online-only Data Supplement.

Multivariable Analysis

Multivariable analysis of recurrence-free survival was performed with the Cox proportional-hazard model. The covariates in the model are described in the Statistical Analysis section. After adjustment for important confounders, type of AF at baseline (HR, 1.35; \( P = 0.043 \)) and LAA isolation strategy (HR, 0.32; \( P = 0.014 \)) during redo were strongly associated with AF recurrence. The HRs and 95% CIs are presented in Table 3.

| Table 1. Baseline Characteristics of Patients in Whom LAA Firing Was Recorded |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                | Group 1 (n=43, 16%) | Group 2 (n=56, 21%) | Group 3 (n=167, 63%) | \( P \) |
| Age, y                         | 61±11            | 61±11            | 64±11            | 0.019           |
| Male, n (%)                    | 32 (74)          | 43 (76)          | 122 (73)         | 0.964           |
| AF type, n (%)                 |                  |                  |                  |                 |
| PAF                            | 12 (28)          | 15 (26)          | 22 (13)          | 0.015           |
| PER                            | 10 (23)          | 14 (25)          | 38 (23)          | 0.978           |
| LSP                            | 21 (49)          | 27 (49)          | 107 (64)         | 0.044           |
| AF duration, mo                | 83±59            | 82±60            | 90±62            | 0.424           |
| BMI, kg/m²                     | 29±6             | 29±6             | 29±5             | 0.403           |
| HTN, n (%)                     | 17 (40)          | 22 (39)          | 78 (47)          | 0.479           |
| DM, n (%)                      | 3 (7)            | 4 (7)            | 13 (8)           | 1.000           |
| Prior CVA, n (%)               | 2 (5)            | 2 (4)            | 10 (6)           | 0.922           |
| CHADS2, n (%)                  |                  |                  |                  |                 |
| 0                              | 12 (28)          | 17 (30)          | 28 (17)          | 0.068           |
| 1                              | 18 (42)          | 22 (39)          | 84 (50)          | 0.306           |
| ≥2                             | 13 (30)          | 17 (30)          | 55 (33)          | 0.918           |
| LA size, mm                    | 40.8±8           | 40.6±7           | 43.2±9           | 0.063           |
| LVEF %                         | 58±8             | 58±8             | 59±7             | 0.577           |
| Follow-up, mo                  | 11±3             | 11±3             | 12±3             | 0.910           |

PAF indicates paroxymal AF; PER, persistent; LSP, long-standing persistent; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CVA, cerebrovascular accident; and LVEF, left ventricular ejection fraction.

Table 2. Recurrences by AF Type

<table>
<thead>
<tr>
<th>AF Type</th>
<th>Group 1 (n=43, n (%))</th>
<th>Group 2 (n=56, n (%))</th>
<th>Group 3 (n=167, n (%))</th>
<th>Log-Rank ( P ) (Comparing Groups 1 Through 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal</td>
<td>3 (9)</td>
<td>3 (8)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Persistent</td>
<td>9 (28)</td>
<td>12 (32)</td>
<td>7 (28)</td>
<td></td>
</tr>
<tr>
<td>Long-standing persistent</td>
<td>20 (63)</td>
<td>23 (60)</td>
<td>17 (68)</td>
<td></td>
</tr>
<tr>
<td>Total recurrences</td>
<td>32 (74)</td>
<td>38 (68)</td>
<td>25 (15)</td>
<td>(&lt;0.001)</td>
</tr>
</tbody>
</table>

TEE Results

LAA mechanical function was evaluated through TTE and TEE assessment in the 204 patients who underwent LAA isolation and were AF free and in the 60 patients who underwent redo LAA isolation. Echocardiographic evaluations were obtained at 3 and 6 months. LAA flow velocity, transmitral E/A ratio, and LAA contractility were determined for each patient. For the purpose of summarizing, E/A ratio and flow velocity were dichotomized at the normal values (≥1.6 and >0.3 m/s, respectively).

A flow velocity >0.3 m/s was recorded in 108 patients (53%; 95% CI 43% to 64%), whereas 110 patients (54%; 95% CI 44% to 65%) demonstrated an E/A ratio ≥1.6. LAA contractility was excellent in 108 patients (53%), and poor contractility was noted in 96 patients (47%). Thrombus formation was not observed in any of the 204 patients. TTE and TEE results with 95% CIs are presented in the left part of Table 4.

Complications

During LAA ablation, 4 (1.8%) pericardial effusions requiring pericardiocentesis occurred. None of the patients required surgery. All patients were discharged after a median hospitalization of 1 day. No phrenic nerve damage was observed.

Discussion

Major Findings

This is the first study demonstrating the LAA as a potential trigger for AF, the prevalence of LAA firing in patients with recurrence of AF/AT after catheter ablation for AF, and the possibility that electric isolation of the LAA can improve success for the treatment of AF during redo procedures.

Anatomic Considerations

The LAA derives from the primordial LA, which is formed mainly by the adsorption of the primordial PVs and their branches. Douglas et al\(^1\) hypothesized that during the incorporation of the PVs into the LA myocardium, the contribution of the vessel wall to the body increases, reducing the component of sinus venosus to a small zone encircling the entrance of the LAA.\(^1\)

The embryological origin suggests that the LAA may initiate AF like the PVs.\(^19\) This could explain the potential active role of the LAA as an underestimated source of AF. Previously, Takahashi et al\(^1^5\) reported on a single case of...
electric disconnection of the LAA for the elimination of foci maintaining AF.

Of note, the ligament of Marshall is an epicardial structure containing sympathetic and parasympathetic nerves. It is in direct connection with the coronary sinus myocardial sleeves and extends in the region between the LAA and the left superior PV. It is conceivable that an abnormal insertion of the ligament of Marshall could be responsible for the observed firing from the LAA.

Another anatomic structure that should be taken into account is the Bachmann bundle. It is generally located in close proximity to the right PVs. Part of the LA architecture, it has several connections with muscle bundles that diverge at the base of the LAA.20 –26 This anatomic connection could explain the rapid activation from the LAA to the septum and right atrium, which could be misleading without direct recording in the LAA during attempts to identify the site of firing.

Previous Studies
Several studies have shown that together with the PVs, many extra-PV areas may be the source of initiation and maintenance of AF.7–14 The most common sites are the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, and LA posterior wall. The reported incidence of extra-PV initiators varies from 3.2% to 47%.7–14

Our study is the first to report firing from the LAA as a possible site of origin of AF in a consecutive series of patients. The prevalence of this finding in our population was 27%. Of these, a smaller group included patients in whom the LAA was the only target of ablation during the procedure. This group accounts for 8.7% of patients. Electric isolation of the LAA required more ablation time compared with isolation of PVs. Our mean radiofrequency time was similar to that described by others.15,20

Similar to what was observed for the isolation of the PVs, isolation of the LAA required either segmental or circumferential lesions. In this respect, our results suggest that isolation of the LAA leads to a higher probability of achieving long-term freedom from AF/AT than focal ablation. These results resemble what was observed several years ago with the PVs.

Because the LAA has a very thin wall and may be prone to perforation, caution should be taken when LAA electric isolation is performed. Indeed, we observed a 1.8% incidence of cardiac tamponade, which was treated with a pericardiocentesis and conservative treatment without any negative sequelae. The management of pericardial effusion was similar to the one occurring after ablation at conventional LA sites.

Postablation Anticoagulation
Because the LAA is a major source of embolic stroke and contributes to the LA mechanical function, discontinuing warfarin after a successful isolation should not be considered. In all successful cases, we performed a TEE 6 months after ablation to assess the contraction and flow velocity of the LAA. Only in cases with adequate LAA flow velocity was
Conclusions

The LAA appears to be responsible for recurrence of AF/tachycardia in at least 27% of patients presenting for repeat procedures. Similar to the PVS, isolation of the LAA can be achieved with segmental lesions, and it is the most effective strategy to achieve freedom from AF, whereas the procedural success rate of focal ablation of the LAA is dismal. The clinical relevance of LAA isolation and its consequences with respect to potential complications requires further investigation.

Disclosures

Drs Al-Ahmad, Burkhardt, Bailey, Sanchez, Cummings, Wang, Schweikert, Hongo, Horton, and Natale report receiving compensation from St. Jude Medical for participation in speakers’ bureaus. Drs Burkhardt, Horton, Sanchez, and Natale report receiving compensation from Biosense Webster for participation in speakers’ bureaus. Drs Burkhardt, Horton, Bailey, Wang, Cummings, Hongo, Al-Ahmad, and Natale report receiving compensation from Medtronic for participation in speakers’ bureaus. Drs Horton, Sanchez, Bailey, Wang, Al-Ahmad, Schweikert, Hongo, Cummings, and Natale report receiving compensation from Boston Scientific for participation in speakers’ bureaus. Drs Horton and Wang report receiving compensation from Hansen Medical for participation in speakers’ bureaus. Drs Schweikert, Hongo, Lewis, and Cummings report receiving compensation from Sanofi-Aventis for participation in speakers’ bureaus. Dr Schweikert reports receiving compensation from Glaxo-Smith-Kline for participation in speakers’ bureau. Dr Wang reports receiving compensation from Lifewatch for participation in speakers’ bureau. Drs Themistoclakis and Bonso report serving as a consultant to or on the advisory board for Hansen Medical and Cyberheart. Dr Al-Ahmad reports serving as a consultant to or on the advisory board for Boston Scientific and Biosense Webster. Drs Lewis and Hongo report serving as a consultant to or on the advisory board for Boston Scientific and Medtronic. Dr Al-Ahmad reports participation in a research grant from Siemens. Dr Natale reports participation in a research grant from St. Jude. The other authors report no conflicts.

References


Several studies have shown that together with the pulmonary veins, many extrapulmonary vein areas may be the source of initiation and maintenance of atrial fibrillation. The most common sites are the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, and left atrial posterior wall. This study is the first to report firing from the left atrial appendage as a possible site of origin of atrial fibrillation in a consecutive series of patients. The prevalence of this finding in our population was 27%, and in 8.7% of patients, the left atrial appendage was the only target of ablation during redo procedures. We performed electric isolation of the left atrial appendage. Similar to what was observed for the isolation of the pulmonary veins, isolation of the left atrial appendage with segmental or circumferential lesions led to a higher probability of achieving long-term freedom from atrial fibrillation/atrial tachyarrhythmia than focal ablation. The clinical relevance of left atrial appendage isolation and its consequences with respect to potential complications require further investigation.

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SUPPLEMENTAL MATERIAL

Supplemental Tables

Table 1: Tukey-Kramer Multiple Comparison Results, Comparing Recurrences among the 3 Groups

<table>
<thead>
<tr>
<th>Groups Compared</th>
<th>Difference Between 2 Compared Proportions</th>
<th>SE</th>
<th>q Statistics</th>
<th>Critical q Values for α = 0.05</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 vs Group 2</td>
<td>4.94</td>
<td>5.46</td>
<td>0.91</td>
<td>3.633</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Group 1 vs Group 3</td>
<td>35.84</td>
<td>2.69</td>
<td>13.32</td>
<td>3.633</td>
<td>&lt;0.05</td>
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<tr>
<td>Group 2 vs Group 3</td>
<td>30.9</td>
<td>5.51</td>
<td>5.61</td>
<td>3.633</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2: Univariate analysis

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Hazard Ratio</th>
<th>95% Hazard Ratio Confidence Level</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Upper</td>
<td>Lower</td>
</tr>
<tr>
<td>Age, years</td>
<td>1.00</td>
<td>0.98</td>
<td>1.01</td>
</tr>
<tr>
<td>Sex</td>
<td>0.75</td>
<td>0.49</td>
<td>1.16</td>
</tr>
<tr>
<td>Duration of AF</td>
<td>1.00</td>
<td>0.99</td>
<td>1.00</td>
</tr>
<tr>
<td>AF type</td>
<td>2.05</td>
<td>1.23</td>
<td>3.39</td>
</tr>
<tr>
<td>BMI</td>
<td>1.00</td>
<td>0.96</td>
<td>1.04</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.30</td>
<td>0.91</td>
<td>1.86</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.54</td>
<td>1.04</td>
<td>2.30</td>
</tr>
<tr>
<td>Prior CVA</td>
<td>0.49</td>
<td>0.18</td>
<td>1.33</td>
</tr>
<tr>
<td>LA size</td>
<td>1.06</td>
<td>0.81</td>
<td>1.39</td>
</tr>
<tr>
<td>LV EF</td>
<td>0.99</td>
<td>0.97</td>
<td>1.02</td>
</tr>
<tr>
<td>CHADS2 Score- 0</td>
<td>0.70</td>
<td>0.47</td>
<td>0.86</td>
</tr>
<tr>
<td>CHADS2 Score- 1</td>
<td>0.94</td>
<td>0.58</td>
<td>1.54</td>
</tr>
<tr>
<td>CHADS2 Score- ≥2</td>
<td>1.77</td>
<td>1.26</td>
<td>2.47</td>
</tr>
</tbody>
</table>

Supplemental Figure Legend for The Movie

Figure 1 (5C supplemental): CARTO movie map. The red dots on the CT represent all the lesions delivered to achieve LAA isolation.