Catheter ablation is recognized as an effective treatment for atrial fibrillation (AF), particularly for paroxysmal AF. Although pulmonary vein isolation (PVI) is widely accepted as the cornerstone of the ablation strategy, alone it is generally considered insufficient for patients with persistent or long-lasting persistent AF. Additional strategies for substrate modification include complex fractionated atrial electrogram (CFAE) ablation, linear ablation (roof and mitral isthmus lines), ganglionic plexi ablation, and targeting of non-PV foci and rotors mapped by novel techniques.

Previous studies have demonstrated the benefit of linear ablation in addition to PVI, especially in patients with persistent AF. However, the recent Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF) II study did not find any incremental benefit of linear ablation; this may be because of potential proarrhythmic effects of incomplete lines as only 74% of lines were successfully blocked. Several meta-analyses suggest that CFAE ablation may be beneficial as an adjunct to PVI. Although studies have reported success using strategies combining linear ablation and CFAE ablation, there are concerns about the potential for proarrhythmia in patients with extensive ablation or linear ablation. There are little data...
WHAT IS KNOWN

- The benefit of complex fractionated atrial electrogram ablation in the treatment of persistent atrial fibrillation is uncertain.

WHAT THE STUDY ADDS

- Complex fractionated atrial electrogram ablation in addition to pulmonary vein isolation and linear ablation did not improve success.
- Complex fractionated atrial electrogram ablation predisposed to recurrent organized atrial tachycardia or flutter.

on the additional effect of CFAE ablation after circumferential PV ablation (CPVA) and complete linear lesion.

This is a multicentre randomized study comparing the strategies of CPVA+linear ablation+CFAE ablation (CFAE arm) versus CPVA+linear ablation (control arm).

Methods

Study Population

This was a prospective, multicentre, randomized controlled trial. Patients, capable of and willing to give consent, with symptomatic persistent or long-lasting persistent AF, presenting for their first catheter ablation procedure were included in this study. They were randomized in a 1:1 fashion to catheter ablation with CPVA and linear ablation (control arm) or CPVA+linear ablation+CFAE ablation (CFAE arm). Sixty-five patients were recruited into each arm from March 2010 to August 2011. Written informed consent was obtained. The study protocol was approved by the Oxford Research Ethics Committee.

Study End Points

The study primary end point was freedom from AF or organized atrial tachycardia (AT) off antiarrhythmic drugs at 12 months after the first ablation procedure based on the absence of documentation on 12-lead ECG and Holter. Secondary end points included 2/multiprocedural ablation procedure based on the absence of documentation on 12-lead ECG and Holter. Second end points included 2/multiprocedural success off antiarrhythmic drugs and AF/AT, procedural characteristics (ie, total ablation time, total procedure time, and rate of termination of AF by ablation), and incidence of adverse events.

Catheter Ablation

The procedures were performed with the patients in the postabsorptive state under general anesthesia. All antiarrhythmic drugs except amiodarone were discontinued for at least 5 half-lives before the procedure. All patients were anticoagulated for at least 1 month, aiming for an internationalized ratio of 2 to 3 on the day of the procedure. They also had transesophageal echocardiography to exclude left atrial (LA) thrombus on the day of the procedure. A heparin bolus and infusion was used to maintain the activated clotting time between 300 and 350 s throughout the procedure. A steerable decapolar catheter (Insquiry; St Jude Medical, St Paul, MN) was positioned within the coronary sinus (CS). Initially, a quadripolar catheter was positioned in the aortic root as a positional reference catheter for the 3-dimensional electroanatomical system (EnSite NavX and Velocity, St Jude Medical). Subsequently, a temperature probe positioned in the oesophagus was used as a positional reference. Transseptal puncture was performed using a Brockenbrough needle through a fixed curve long sheath (SL(0); St Jude Medical) with the aid of fluoroscopy. A wire was introduced into the left-sided PVs, and the SL(0) sheath was pulled back. An F-curve 3.5-mm irrigated-tip catheter (ThermoCool; Biosense Webster, Diamond Bar, CA) was then manipulated manually to cross the septum via the hole created by the previous transseptal puncture using the wire as a guide. Subsequently, a circular multipolar mapping catheter (Optima or AFocus II, St Jude Medical) was introduced via the SL(0) sheath into the LA.

An electroanatomical shell of the LA was created (EnSite NavX and Velocity, St Jude Medical). All patients had ipsilateral PVs isolated in pairs by CPVA as described before, followed by linear ablation during AF. Roof line ablation was performed by creation of a contiguous line of ablation lesions from the left to right superior PVs over the most cranial portion of the LA roof. Our technique for mitral isthmus ablation has been described elsewhere. Briefly, mitral isthmus ablation was performed by drag ablation starting from a lateral position (3–4 o’clock) on the mitral valve annulus to the isolated left inferior PV. Subsequently, CFAE ablation was performed guided by CFAE maps in patients randomized to the CFAE arm. After restoring sinus rhythm either through ablation or electric cardioversion, the lines were checked for bidirectional block. If not blocked, further ablation (including CS ablation for the mitral isthmus line) was performed to achieve block. Lines were retested for block after a 30-minute wait.

CFAE Mapping and AF Cycle Lengths

The technique of acquiring CFAE maps using an automated algorithm (EnSite NavX; St Jude Medical) has been previously described and validated. In short, high-frequency atrial electrograms acquired using the circular multipolar catheter were analyzed to compute the mean cycle length between the multiple deflections over a specified period of time (CFAE mean). The CFAE mean was then represented on the geometric shell as a color-coded display. CFAE areas were defined as sites having a CFAE mean of <120 ms. The recommended CFAE mean tool settings were peak-to-peak sensitivity of 0.03 to 0.05 mV (to avoid sensing noise), electrogram refractory period of 35 to 45 ms (<30 ms is regarded as nonphysiological), electrogram width of <10 ms (avoid detecting farfield signals), electrogram segment length of 5 s, and interpolation and internal/external projection of <10 mm (to avoid electrograms from electrodes, which are not in good contact).

A dense CFAE map was made (minimum 400 points) ensuring adequate and even coverage of the entire LA and CS. CFAE maps were acquired at baseline, post CPVA, post CPVA, and lines. At these time points, mean LA appendage (LAA) cycle lengths and right atrial (RA) appendage/CS cycle lengths were computed over 10-s segments.

Ablation End Points and Parameters

The end point of CPVA was complete PV isolation with entrance and exit block as assessed with the aid of circular multipolar catheter. The end point of linear ablation was complete bidirectional block. The multipolar catheter was positioned in the LAA for pacing to assess for roof and mitral isthmus block. Bidirectional block was verified by activation mapping, differential pacing, and mapping for widely spaced double potentials along the line. CFAE ablation aimed to eliminate or organize local electrograms, usually necessitating 30 to 60 s of radiofrequency energy delivery at each site. The overall end point of CFAE ablation was elimination of CFAE areas demonstrated by a repeat CFAE map after CFAE ablation (Figure 1).

For each lesion, ablation was typically performed for ≤30 s on the posterior LA wall and 60 s at other sites. Maximum ablation powers were 30 W for PVI; 30 W for roof; 40 W (annular end), 30 W (PV end), and 30 W (CS) for mitral isthmus; and 30 W for CFAE. Temperature was limited to 48°C, and irrigation rate was between 17 and 30 mL/min for both groups.

Ablation Strategy at Redo Procedures

At the first redo procedure, the strategy used during the index procedure was preserved. In the CFAE arm, patients presenting with AF first had reisolation of reconnected PVs, followed by CFAE ablation, and lines were checked after restoration of sinus rhythm. In the
control arm, patients presenting with AF had reisolation of reconnected PVs followed by electric cardioversion and checking of lines. Presenting AT and any sustained organized AT induced during the procedure were mapped and ablated. Induction was not done routinely. CFAE ablation was performed at the discretion of the operator for patients in the control arm at subsequent redo procedures.

Follow-Up
All patients had echocardiographic examination immediately after the procedure. Antiarrhythmic medications were stopped 2 to 3 months after the procedure. They were followed up at our center at 3 months with 12-lead ECG and at 12 months with ECG and ambulatory monitoring as per the Heart Rhythm Society/European Heart Rhythm Association/European Commission Authentication Service consensus guidelines. They were also followed up every 3 months in their local referring centers for the first year. Subsequently, they had 6 months of follow-up with 12-lead ECGs both at our center and their local referring centers. They were assessed earlier if they had symptoms. All patients had direct access to specialist arrhythmia nurses. Ambulatory ECG monitoring was arranged if they had symptoms. Any episode of symptomatic or asymptomatic atrial arrhythmia documented on ECG or Holter monitor after the 3-month blanking period constituted recurrence.

Statistical Analysis
Continuous variables are expressed as mean±SD unless otherwise stated. Normally distributed parameters were compared using unpaired t tests and 1-way ANOVA. Nonparametric data were compared using Mann Whitney U test. Categorical variables expressed as numbers or percentages were analyzed using the Fisher exact test. Kaplan–Meier method and Log-rank test were used to analyze and compare procedural success or arrhythmia-free survival. Univariate and multivariate analyses using logistic regression were used to evaluate variables for predicting procedural success. Logistic models were adjusted for age, sex, body mass index, the presence of cardiovascular disease, AF type, AF duration, duration of maintenance of sinus rhythm after cardioversion, CHA2DS2-VASc score, LA size, left ventricular function, CFAE ablation, baseline LAA cycle length, termination by ablation, and direct current cardioversion in the blanking period. All tests were 2-tailed, and statistical significance was established at P<0.05. Analyses were performed using StatView and GraphPad Prism version 4.0.

Sample size calculation was based on survival analysis with a power of 80% and 2-tailed significance of 0.05 to detect an absolute 25% difference in primary outcome (40% single-procedural success for the control arm at 12 months).

Results
A total of 131 patients were recruited. Sixty-six patients were randomized to CPVA and linear ablation, including roof and mitral isthmus lines (control arm). Sixty-five patients were randomized to further CFAE ablation after CPVA and linear ablation (CFAE arm).

Baseline Clinical Characteristics
The mean age was 61±10 years, 75% were men, all patients had persistent AF (42% had long-lasting persistent AF) with a median duration of 2 years, 68% had associated cardiovascular
comorbidities, mean LA size was 46±6 mm, and 38% had been prescribed amiodarone before their procedure. There were no significant differences in baseline clinical characteristics between the 2 arms (Table 1).

**Procedural Results**

The overall procedure and ablation times were significantly longer in the CFAE arm: 201±35 versus 152±45 minutes \((P<0.0001)\) and 70±20 versus 55±17 minutes \((P=0.0003)\), respectively. This was because of mean CFAE ablation time of 20±12 minutes. PVI and roof block were achieved in all patients. Mitral isthmus block was achieved in 95% (123/130) of patients. CS ablation was performed in 90 of 130 patients (69%). There was a trend toward a higher incidence of AF termination to sinus rhythm (directly or via AT) in the CFAE arm (26% versus 12%; \(P=0.07\); Table 2).

<table>
<thead>
<tr>
<th>Table 1. Patients Baseline Characteristics</th>
<th>Overall (n=130)</th>
<th>CFAE (n=65)</th>
<th>Non-CFAE (n=65)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61±10</td>
<td>61±11</td>
<td>61±9</td>
<td>0.94</td>
</tr>
<tr>
<td>Male (%)</td>
<td>98 (75)</td>
<td>50 (77)</td>
<td>48 (74)</td>
<td>0.69</td>
</tr>
<tr>
<td>Cardiovascular disease (%)</td>
<td>89 (68)</td>
<td>43 (66)</td>
<td>46 (71)</td>
<td>0.58</td>
</tr>
<tr>
<td>Long-lasting persistent AF</td>
<td>54 (42)</td>
<td>24 (37)</td>
<td>30 (46)</td>
<td>0.38</td>
</tr>
<tr>
<td>Median duration of continuous AF, y</td>
<td>2 (&lt;1–8)</td>
<td>2 (&lt;1–6)</td>
<td>2 (&lt;1–8)</td>
<td>0.89</td>
</tr>
<tr>
<td>CHADS2-VASc score (median)</td>
<td>2 (0–5)</td>
<td>2 (0–4)</td>
<td>2 (0–5)</td>
<td>0.81</td>
</tr>
<tr>
<td>BMI</td>
<td>30.9±5.3</td>
<td>30.2±6.0</td>
<td>31.6±4.6</td>
<td>0.23</td>
</tr>
<tr>
<td>LA size</td>
<td>46±6</td>
<td>45±6</td>
<td>46±7</td>
<td>0.35</td>
</tr>
<tr>
<td>Impaired LV function (&lt;40%)</td>
<td>28 (22)</td>
<td>13 (20)</td>
<td>15 (23)</td>
<td>0.35</td>
</tr>
<tr>
<td>Amiodarone use</td>
<td>50 (38)</td>
<td>21 (32)</td>
<td>29 (45)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

\(AF\) indicates atrial fibrillation; BMI, body mass index; CFAE, complex fractionated atrial electrogram; LA, left atrium; and LV, left ventricle.

<table>
<thead>
<tr>
<th>Table 2. Comparison of Ablation/Procedural Data</th>
<th>CFAE (n=65)</th>
<th>Non-CFAE (n=65)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total procedure time, min</td>
<td>201±35</td>
<td>152±45</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total ablation time, min</td>
<td>70±20</td>
<td>55±17</td>
<td>0.0003</td>
</tr>
<tr>
<td>Total fluoroscopy time, min</td>
<td>47±22</td>
<td>39±13</td>
<td>0.03</td>
</tr>
<tr>
<td>LPV ablation time, min</td>
<td>15±5</td>
<td>17±8</td>
<td>0.12</td>
</tr>
<tr>
<td>RPV ablation time</td>
<td>14±7</td>
<td>14±8</td>
<td>0.93</td>
</tr>
<tr>
<td>Percentage PVI</td>
<td>100 (65/65)</td>
<td>100 (65/65)</td>
<td>NS</td>
</tr>
<tr>
<td>Percentage of roof block</td>
<td>100 (65/65)</td>
<td>100 (65/65)</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral isthmus ablation time, min</td>
<td>13±7</td>
<td>14±7</td>
<td>0.81</td>
</tr>
<tr>
<td>Endocardial</td>
<td>10±5</td>
<td>11±5</td>
<td>0.59</td>
</tr>
<tr>
<td>CS</td>
<td>6±4</td>
<td>6±4</td>
<td>0.93</td>
</tr>
<tr>
<td>Percentage of CS ablation to achieve block</td>
<td>66 (40/61)</td>
<td>69 (43/62)</td>
<td>0.70</td>
</tr>
<tr>
<td>Percentage of mitral isthmus block</td>
<td>94 (61/65)</td>
<td>95 (62/65)</td>
<td>1.0</td>
</tr>
<tr>
<td>CFAE ablation time, min</td>
<td>20±12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage termination</td>
<td>26 (17/65)</td>
<td>12 (8/65)</td>
<td>0.07</td>
</tr>
<tr>
<td>LAA CL (baseline)</td>
<td>160±23</td>
<td>155±23</td>
<td>0.45</td>
</tr>
<tr>
<td>RAA CL (baseline)</td>
<td>173±31</td>
<td>163±26</td>
<td>0.19</td>
</tr>
<tr>
<td>LAA CL (post PVI)</td>
<td>165±26</td>
<td>164±20</td>
<td>0.93</td>
</tr>
<tr>
<td>RAA CL (post PVI)</td>
<td>186±34</td>
<td>174±30</td>
<td>0.32</td>
</tr>
<tr>
<td>LAA CL (post linear ablation)</td>
<td>166±21</td>
<td>179±35</td>
<td>0.12</td>
</tr>
<tr>
<td>RAA CL (post linear ablation)</td>
<td>186±38</td>
<td>183±36</td>
<td>0.81</td>
</tr>
<tr>
<td>LAA CL (post CFAE ablation)</td>
<td>179±28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAA CL (post CFAE ablation)</td>
<td>191±35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CFAE indicates complex fractionated atrial electrogram; CS, coronary sinus; LAA CL, left atrial appendage cycle length; LPV, left pulmonary vein; NS, not significant; PVI, pulmonary vein isolation; RAA CL, right atrial appendage cycle length; and RPV, right pulmonary vein.
There were no significant differences in the LAA and RA appendage/CS cycle lengths at baseline and at each stage of the ablation procedure, that is, post PVI and post linear ablation. Overall, there was a steady increase in LAA cycle length from 158±23 ms at baseline, 165±24 ms post PVI, 172±29 ms post linear ablation, to 179±28 ms post CFAE ablation \((P=0.0007; 1\text{-way ANOVA})\). The same was true for RA appendage/CS cycle length (168±29 ms, 181±33 ms, 185±37 ms, and 191±35 ms; 1\text{-way ANOVA}; \(P=0.01\); Figure 2).

**Acute Complications**

Four patients had femoral artery pseudoaneurysms (3 treated with thrombin injection and 1 required surgery because of the presence of arteriovenous fistula). These patients had femoral arterial access initially (Methods section). One patient had cardiac tamponade who responded to pericardiocentesis. One patient had a transient ischemic attack after the second ablation procedure. One patient had a deep vein thrombosis despite therapeutic international ratio. Finally, one patient died of possible atrio–oesophageal fistula at 30 days post ablation (control arm), although postmortem did not definitively confirm the diagnosis (this patient was excluded from the analysis).

There was no significant difference in the complication rate between the 2 arms.

**Outcomes After the First Procedure**

There was no significant difference in the outcome between the CFAE and control arms (46% [30/65] versus 57% [37/65]; \(P=0.20\)) at 12 months after the first procedure (Figure 3).

Eleven of 74 patients (15%) had late recurrences (13–22 months) making the overall single-procedural success rate in the CFAE and control arms (39% [25/65] versus 48% [31/65]; \(P=0.38\)). Four of the 11 late recurrences had paroxysmal AF.

Thirty patients (46%) in the CFAE arm had direct current cardioversion for early recurrence of AF/AT in the blanking period compared with 19 patients (29%) in the control arm (\(P=0.07\)).

Thirty-four of 40 patients (CFAE arm) and 31 of 34 patients (control arm) had redo procedures. Four patients experienced a significant improvement of their symptoms, that is, paroxysmal AF under control with medications, and chose not to undergo further ablation treatment.

**Findings at the First Redo Procedure**

In the CFAE arm, 23 patients had documented organized AT/flutter only, 9 patients had AF only, and 2 patients had both. In the control arm, 9 had AT/flutter only, 20 had AF (5 paroxysmal AF), and 2 had both. Patients in the CFAE arm tended to present with AT/flutter, whereas the mode of recurrence in the control arm was predominantly AF, \(P=0.008\) (Figure 4A). Of the 25 patients with the recurrence of AT/flutter in the CFAE arm, 11 had documented AT only, 10 had macro–re-entrant flutters, and 4 had both. Of the 11 patients in the control arm, 8 had AT only, 2 had flutters, and 1 had both (Figure 4B). A total of 37 AT/flutter were treated in the CFAE arm (21 ATs, 7 cavotricuspid isthmus flutters, 7 mitral isthmus flutters, and 2 roof flutters) compared with 14 in the control arm (10 ATs, 2 cavotricuspid isthmus flutters, 1 mitral isthmus flutter, and 1 roof flutter; Figure 4C).

The locations of the 31 ATs are depicted in Figure 5. Nineteen were mapped to the LA (anterior wall, 7; LAA ostium, 3; posterior wall, 4; septum, 2; LA floor, 1; left inferior PV, 1; and right inferior PV, 1). Ten were mapped to the RA (CS os, 6; RA appendage os, 2; superior vena cava junction, 1, and lateral wall, 1). Two ATs terminated before mapping.

The percentage of PV reconnection was not significantly different in both CFAE and control arms (51% [69 of 136 PVs] versus 60% [75 of 124 PVs]; \(P=0.13\)). Reconnection rates were also not significantly different across roof lines (41% [14/34] versus 29% [9/31]; \(P=0.31\)) and mitral isthmus
lines (56% [19/34] versus 61% [19/31]; P=0.62). There was a significantly higher incidence of gap-related flutter (defined as flutter secondary to gaps in the previous linear ablation) in the CFAE arm (26% [9/34] versus 3% [1/31]; P=0.01; Figure 4D).

Outcomes After Multiple Redo Procedures

The outcomes after each ablation procedure are summarized in Figure 6. Only patients who had at least 12 months of follow-up after their last procedures were included in the analysis. After 2 procedures, there was no difference in the success rate in the CFAE and control arms (71% [46/65] versus 72% [47/65]; P=1.0). Ten patients (15%) in the control arm eventually had CFAE ablation in their third or fourth procedure. After multiple procedures and a mean follow-up duration of 35±5 months, the success rate in the CFAE arm was also not significantly different from that of the control arm (78% [51/65] versus 80% [52/65]; P=1.0).

Predictors of AF/AT Recurrence

Univariate and multivariate analyses for predictors of procedural success were summarized in Table I in the Data Supplement. Only early recurrence of AF/AT was a consistent multivariate predictor for late recurrence.

Discussion

Main Findings

The main findings are summarized below:

Additional CFAE ablation did not improve single-procedural success at 12 months (46.2% [30/65] versus 56.9% [37/65]; P=0.20) and multiprocedural success (78% [51/65] versus 80% [52/65], P=1.0) despite significantly longer procedure and ablation times (201±35 versus 152±45 minutes; P<0.0001 and 70±20 versus 55±17 minutes; P=0.0003, respectively).

The mode of recurrence after CFAE ablation was predominantly organized AT/flutter (P=0.0008).

There was a significantly higher incidence of gap-related flutter in the CFAE arm (26% [9/34] versus 3% [1/31]; P=0.01).

Rationale of the Reversed Stepwise Approach

Catheter ablation strategies comprising adjuvant CFAE ablation are commonly reported in the literature. The
Bordeaux stepwise approach suggested PVI followed by CFAE ablation before linear ablation, partly because of the challenging nature of achieving successful mitral isthmus ablation, hence leaving it to the end. Knecht et al\(^{17}\) reported that most patients eventually needed linear ablation using this approach.

There is a growing body of evidence that PVI or linear ablation reduces CFAE areas, even in sites remote from the ablation.\(^{18,19}\) This would imply that a strategy which targets CFAE ablation last (reversed stepwise approach), after PVI and linear ablation could limit unnecessary CFAE ablation. This study is also unique in that a CFAE mean map is acquired after ablating the CFAE areas, in an attempt to provide objective evidence of elimination of CFAE areas.

**Literature Review**

The single- and multi-procedural success rates in this study are comparable with those published previously. An approach using PVI and CFAE ablation has been reported as producing success rates of 29\% to 74\% after single procedure.\(^{7,20-25}\) Oral et al,\(^{20}\) Elayi et al,\(^{25}\) Han et al,\(^{24}\) and Wang et al\(^{23}\) recruited patients with long-lasting persistent AF, whereas Verma et al\(^{21}\) included patients with paroxysmal AF in the STAR AF study. PVI and linear lesions had a success rate of 37\% to 74\% after a single procedure.\(^{22,24-26,28}\) Combining PVI, CFAE, and linear ablation, Wang et al\(^{23}\) reported single-procedural success of 51\% to 54\%, whereas Lin et al\(^{28}\) reported 70\%. Using the Bordeaux stepwise approach, O’Neill et al\(^{29}\) reported a need for redo procedures in 52\% of patients.

Our results compliment those of a recent study (2C3L) comparing PVI and linear ablation with PVI, linear ablation, and CFAE ablation.\(^{30}\) In their study, the authors also included a cavotricuspid isthmus line in their lesion set. Their 12-month single-procedural success rates were 60\% versus 67\%. This was in spite of the higher rate of termination in the stepwise approach arm (53\% versus 21\%). Although lower termination rates of 26\% versus 12\% were reported in our study, this was likely because of difference in patient characteristics, particularly our longer duration of AF before ablation.

**Conventional CFAE Ablation Predisposes to Gap-Related Flutter**

When asking why additional CFAE ablation does not increase success rates, it is important to understand the mechanisms of arrhythmia recurrence. The incidence of PV reconnection in both arms of patients undergoing repeat procedures was similar, suggesting that the failure to abolish triggers may be the main cause of recurrent arrhythmias. Modern surgical ablation, where permanent PVI is easier to achieve, has reported higher single-procedural success rates than catheter ablation.\(^{31}\)

In our study, the additional CFAE ablation prevented AF recurrence at the expense of causing more micro–re-entrant and macro–re-entrant flutters. By forming islands of noncontiguous lesions, extensive CFAE ablation may create areas of slow conduction within the LA, leading to a wider excitable gap and predisposing to macro–re-entrant flutter in the presence of gaps in lines, thereby increasing the proarrhythmic potential (26\% versus 3\%; \(p=0.03\)).\(^{32}\) Using the Bordeaux stepwise approach, the incidence of postablation AT was \approx 50\%. A recent meta-analysis identified adjunctive CFAE ablation as a risk for factor for postablation ATs (risk ratio, 1.77).\(^ {32}\)

Successful CFAE ablation is based on the assumption that the fractionated electrograms represent fixed anatomic areas that are critical to the maintenance of AF. Identifying these areas remains challenging, and it is only recently that more sophisticated mapping technologies to perform phase mapping show promise.\(^8,33\) Indeed, understanding the electrophysiologic substrate may potentially avoid the need for linear lesions.

**Recommendations**

As with PVI, a successful linear lesion strategy is dependent on durable lesions and long-term conduction block. In this study, there was a 100\% success rate at achieving acute roof line block and a 95\% success rate at achieving acute mitral isthmus block. These success rates are higher than many previously reported series and may represent the use of high powers, irrigated-tip catheters, steerable sheath technology, and the use of epicardial ablation in the distal CS.\(^{14,34}\) However, despite the high acute success rates, there was still a moderately high reconduction rates seen at redo procedures. Other studies found increased proarrhythmia secondary to...
resumption of conduction in linear lesions. The recent STAR AF II study has also questioned the benefit of additional ablation beyond PVI.\textsuperscript{15} Until ablation techniques and technology improve in the future, it may be prudent to focus the ablation efforts on the strategy, which clearly affects outcome, that is, achieving durable PVI.

Limitations
Although the study complied with the American Heart Association/American College of Cardiology/European Society of Cardiology guidelines, asymptomatic episodes may have been missed, which would have been picked up by implantable monitoring devices; however, documented sinus rhythm at regular intervals in this group of patients with highly persistent/long-lasting persistent AF initially would indicate a significant improvement of AF burden. In our ablation strategy, CFAE ablation is limited to the LA and CS. Previous studies have shown conflicting results of added right-sided CFAE ablation. The STAR AF II study also did not show any benefit of RA and LA CFAE ablation. The high rates of reconnection across empirical PVI and linear lesions (≤60%) also make it difficult to assess the true effect of additional CFAE ablation. Finally, there is relatively low rate of AF termination to sinus rhythm in both arms of the study. Although this may suggest that critical AF drivers were not ablated, it may also be because of the fact that the study cohort consisted of patients with highly persistent/long-lasting persistent AF with high incidence structural heart disease. Moreover, the multiprocedural success rate was not compromised.

Conclusions
CFAE ablation did not confer additional benefit when performed in addition to CPVA and linear ablation. In fact, it may be proarrhythmic, resulting in more gap-related macro-reentrant flutters. Early recurrence of AT/AF is an independent predictor of procedure failure.

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References
collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). Endorsed and approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society. 


No Benefit of Complex Fractionated Atrial Electrogram Ablation in Addition to Circumferential Pulmonary Vein Ablation and Linear Ablation: Benefit of Complex Ablation Study


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**SUPPLEMENTAL MATERIAL**

**Supplemental Table:** Regression analysis of variables for predicting success after single ablation procedure, 2 ablation procedures and multiple ablation procedures for the treatment of persistent atrial fibrillation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Single procedural success</th>
<th>Success after 1 or 2 procedures</th>
<th>Multi-procedural success</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate analysis</td>
<td>Multivariate analysis</td>
<td>Univariate analysis</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>Odds ratio</td>
<td>P value</td>
</tr>
<tr>
<td>Age</td>
<td>0.20</td>
<td>0.98 (0.94-1.01)</td>
<td>0.07</td>
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<tr>
<td>Male sex</td>
<td>0.37</td>
<td>1.45 (0.64-3.28)</td>
<td>0.01</td>
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<tr>
<td>BMI&gt;30</td>
<td>0.16</td>
<td>1.88 (0.77-4.55)</td>
<td>0.24</td>
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<tr>
<td>Cardiovascular disease</td>
<td>0.04</td>
<td>0.46 (0.22-0.98)</td>
<td>0.17</td>
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<tr>
<td>CHA2DS2-Vasc score</td>
<td>0.14</td>
<td>0.82 (0.63-1.07)</td>
<td>0.002</td>
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<tr>
<td>Long-lasting persistent AF</td>
<td>0.13</td>
<td>0.57 (0.28-1.17)</td>
<td>0.24</td>
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<tr>
<td>History of AF (years)</td>
<td>0.22</td>
<td>0.94 (0.84-1.04)</td>
<td>0.20</td>
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<tr>
<td>SR&gt;2 weeks after DCCV</td>
<td>0.16</td>
<td>1.71 (0.81-3.58)</td>
<td>0.47</td>
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<tr>
<td>LA size</td>
<td>0.53</td>
<td>1.02 (0.96-1.08)</td>
<td>0.32</td>
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<tr>
<td>Impaired LV f(n)</td>
<td>0.98</td>
<td>1.01 (0.44-2.36)</td>
<td>0.75</td>
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<tr>
<td>CFAE ablation</td>
<td>0.29</td>
<td>0.69 (0.34-1.38)</td>
<td>0.96</td>
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<tr>
<td>LAA cycle length</td>
<td>0.16</td>
<td>1.02 (0.99-1.04)</td>
<td>0.41</td>
</tr>
<tr>
<td>Termination during ablation</td>
<td>0.02</td>
<td>2.71 (1.16-6.36)</td>
<td>0.22</td>
</tr>
<tr>
<td>DCCV during blanking period</td>
<td>&lt;0.0001</td>
<td>0.17 (0.17-0.40)</td>
<td>0.0006</td>
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</tbody>
</table>