Electrogram-guided substrate ablation with or without pulmonary vein isolation in patients with persistent atrial fibrillation

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Aims Ablation of complex fractionated atrial electrograms (CFAEs) is a new approach for the treatment of atrial fibrillation (AF). The purpose of the study was to assess the efficacy of CFAE ablation as a stand-alone strategy in patients with persistent AF and to compare it with a combined approach of CFAE ablation and pulmonary vein isolation (PVI).

Methods and results The study included 77 consecutive patients with persistent AF who underwent radiofrequency (RF) ablation of CFAE as a sole ablation procedure (CFAE group, n = 23 patients) or a combined approach of CFAE ablation and PVI (CFAE plus PVI group, n = 54 patients). Procedures were guided by three-dimensional mapping systems. After the procedure, AF recurrences were evaluated with 7-day Holter recordings at 1, 3, and 6 months and every 6 months thereafter. Treatment failure was defined as ≥1 AF episode lasting >30 s on Holter recordings during follow-up. After a mean follow-up time of 13 ± 10 months, 2 of 23 patients (9%) with CFAE ablation and 22 of 54 patients (41%) with CFAE plus PVI were in sinus rhythm after a single ablation procedure without anti-arrhythmic medication (P = 0.008).

Conclusion Ablation of CFAE as a stand-alone ablation strategy seems insufficient for the treatment of patients with persistent AF. Pulmonary vein isolation plus CFAE ablation significantly increases the midterm success rate.

KEYWORDS Persistent atrial fibrillation; Ablation; Pulmonary vein isolation; Complex fractionated atrial electrograms

Introduction

Most ablation strategies for atrial fibrillation (AF) include pulmonary vein (PV) isolation.1–4 Ablation of complex fractionated atrial electrograms (CFAEs) has recently been used in patients with AF for encouraging initial results even as a solitary ablation procedure.5 Atrial fractionated potentials are thought to indicate areas of non-uniform wavelet propagation and slowed conduction that may be implicated in the perpetuation of AF.6 Therefore, CFAEs have been targeted to modify the substrate implicated in the maintenance of AF.5 In a recent study by Oral et al.,7 which included patients with chronic AF, CFAE ablation had a relatively low success rate (33%) and a second ablation procedure was often required. The study strongly suggested that omission of pulmonary vein isolation (PVI) is a major limitation of this ablation strategy. Moreover, prior studies have suggested that single procedures of PVI seem to be rather ineffective in patients with persistent AF as well.8

The purpose of the study was to assess the efficacy of CFAE ablation as a stand-alone strategy and to compare it with that of PVI plus CFAE ablation in patients with persistent AF. Using existing information, it was hypothesized that CFAE ablation is moderately effective as a stand-alone ablation approach in treating patients with persistent AF.

Methods

Patient characteristics

The study included 77 consecutive patients with persistent AF who underwent RF ablation of CFAEs as a sole ablation procedure (CFAE group, n = 23 patients) or a combined approach of CFAE...
ablation plus PVI (CFAE plus PVI group: n = 54 patients). Enrolled patients had to meet the following criteria: (i) they should have had at least two failed attempts of anti-arrhythmic drug therapy, and (ii) persistent AF lasting for at least 1 month before the ablation procedure. Patients were considered for the ablation procedure only if they were symptomatic and had failed conventional anti-arrhythmic drug therapy, electrical cardioversion, or both. Patients with left atrial (LA) enlargement of >60 mm were excluded from the study.

The use of CFAE ablation either as a stand-alone strategy or combined with PVI ablation was based on the operator’s discretion, but the decision was not guided by patients’ characteristics. Complex fractionated atrial electrogram ablation as a stand-alone procedure was performed in the first 12 consecutive patients. After the automated signal analysis, algorithms became available for another 11 patients who underwent CFAE ablation only.

Electrophysiological study
All anti-arrhythmic medications were discontinued for at least 4–5 half-lives prior to the procedure with the exception of amiodarone. Uninterrupted oral anticoagulation (INR 2–3) was administered for at least 1 month before the procedure, and transesophageal echocardiography was performed to rule out atrial thrombi.

After written informed consent, patients underwent electrophysiological study under conscious sedation with midazolam and fentanyl. Access was obtained through both femoral vessels. An octopolar electrode catheter (XPTM, C.R. Bard) was positioned within the coronary sinus (CS). Following trans-septal puncture, two steerable catheters were positioned in the LA under the guidance of trans-septal sheaths (Preface Multipurpose, Biosense Webster, Diamond Bar, CA, USA; SLO or SL1 or Agilis St Jude Medical, St Paul, MN, USA). An irrigated-tip ablation catheter (Celsius Thermocool, Biosense Webster or Therapy Cool Path open-irrigated Catheter, St Jude Medical) was used in combination with the NavX system (St Jude Medical) or a NaviStar Thermo-Cool, Biosense Webster catheter in combination with the CARTO system (Bio- sense Webster). In addition, a circular mapping catheter equipped with 10 or 14.1 mm electrodes (Lasso, Biosense Webster or Orbiter PV, C.R. Bard) was used. After trans-septal catheterization, systemic anticoagulation was achieved with intravenous heparin maintaining an activated clotting time of 280–320 s. Pre-ablation and post-ablation PV angiograms were performed.

Complex fractionated atrial electrogram ablation
Following the description by Nademanee et al., 5 CFAEs were defined as multi-component atrial electrograms including (i) atrial electrograms with two or more deflections and/or perturbation of the baseline and/or continuous electrical activity over 10 s or (ii) atrial electrograms with a very short cycle length (CL) (<120 ms) over 10 s. Initially, CFAEs were defined by visual inspection and by using automated signal analysis algorithms when they became available. Using the CARTO system, 2.5 s bipolar electrogram recordings at each endocardial location sampled before ablations were analysed with the custom software embedded in the CARTO XP mapping system (CFAE Software Module, CARTO XP System, Biosense Webster, Inc.). In the NavX system, the algorithm measures the time between multiple, discrete deflections (dV/dt) in a local AF electrocardiogram recordings over a specified length of time (5 s) and then averages these inter-deflection time intervals to calculate a mean CL of the local electrogram during atrial fibrillation (AF) (CFAE Software; Ensite NavX; St Jude Medical; Minneapolis, MN, USA). In 23 of 54 patients (42.6%) of the CFAE plus PVI group (CARTO Software Module n = 4; CFE Software; Ensite NavX n = 19) and in 10 of 23 patients (43.5%; P = 0.94) of the CFAE group (Ensite NavX system n = 10), an automated signal analysis algorithm was used (Figure 1).

The left and, subsequently, the right atrium were screened for fragmented electrograms, which were ablated if detected. The atria are divided into nine segments for defining the CFAE regions: (i) septum including the Bachman-bundle region; (ii) left posterior mitral annulus; (iii) CS; (iv) PV region; (v) roof of the LA; (vi) anterior mitral annulus; (vii) cavotricuspid right atrial isthmus; (viii) crista terminalis; and (ix) right and left atrial appendages.

Radiofrequency energy was delivered for <2 min at each CFAE ablation site with a maximal power of 35 W at the anterior LA wall and 30 W at the posterior LA wall (flow rate of 20–30 mL/min and maximum temperature 43°C). Radiofrequency current was delivered continuously until electrically silent spots were created. The ablation within the CS was performed using limited power (maximum of 25 W and irrigation rate of 20 mL/min) and was restricted to the proximal part.

The primary procedural endpoint was either complete elimination of all targeted CFAEs or conversion of AF to normal sinus rhythm. If AF had only regularized (e.g. to atrial flutter or atrial tachycardia) after the completion of CFAE ablation, tachycardia was mapped (Figure 2). Ablation was performed if a macro-re-entrant mechanism was detected (e.g. cavotricuspidal- or mitral isthmus-dependent). If the arrhythmia was of micro-re-entrant or focal origin, external cardioversion was performed. If AF persisted at the end of the ablation procedure, external cardioversion was used to restore sinus rhythm.

Pulmonary vein isolation
Pulmonary vein isolation was performed as an initial ablation step in all patients of the CFAE plus PVI group as previously described.9 Ablation was guided by circumferential mapping or anatomical three-dimensional reconstruction of LA and PV using the CARTO (Biosense Webster) or NavX-System (St Jude Medical). Both mapping systems were equipped with image integration software. Radiofrequency energy through the 3.5 mm irrigated-tip catheter with a flow rate of 20–30 mL/min was delivered for <2 min for lesions to isolate the PV (maximum temperature 43°C and maximum power 30 W). The endpoint of PV ablation was electrical isolation signified by the abolition or dissociation of PV potentials. Routinely, all PVS were targeted for electrical isolation.

Post-ablation management and follow-up
Patients remained hospitalized under continuous rhythm monitoring for at least 2 days after the procedure. Heparin infusion was continued until the international normalized ratio was ≥2. No anti-arrhythmic drugs were prescribed except amiodarone in patients with highly symptomatic AF recurrence only for the 4 weeks post-ablation. If no AF recurrence was detected within the first 6 months after ablation, coumadin was discontinued. A repeat ablation procedure was offered to patients in case of symptomatic AF recurrence beyond the third month after ablation.

Patients were seen in the outpatient clinic at 1, 3, and 6 months after the initial ablation procedure and every 6 months thereafter. The follow-up was performed according to the recommendations of the German Atrial Fibrillation Competence Network and the European Heart Rhythm Association on outcome parameters for trials in AF.6 Recurrence of AF or atrial flutter within the first weeks after ablation was considered transient,8 and a blanking period of 4 weeks was applied. For documentation of arrhythmia recurrences, a 7-day Holter recording was used at each of the follow-up visits. The long-term success was defined as stable sinus rhythm without AF episodes (lasting longer than 30 s), sustained atrial flutter, or atrial tachycardia. At 3 and 12 months after the ablation procedure, all patients underwent magnetic resonance imaging (MRI) or computed tomography (CT) to exclude PV stenosis.

Statistical analysis
Data are expressed as mean ± SD, median (25th–75th percentiles), or number of patients (%). Comparisons between groups were made by χ² test or Fisher’s exact test for categorical variables and...
Figure 1  Posterior (left) and anterior (right) view of a three-dimensional shell of the left atrium reconstructed with the Ensite NavX system. The algorithm measures the time between multiple, discrete deflections in a local atrial fibrillation electrocardiogram recorded over 5 s and then averages these inter-deflection time intervals to calculate a mean cycle length of the local EGM during atrial fibrillation. This mean cycle length is then projected onto the left atrial anatomical shell as a colour-coded display. The shorter the cycle length, the more rapid and fractionated is the local electrocardiogram. Areas shaded in red and white represent areas with a average cycle length of < 80 ms (scale on left side of figure) or regions with very rapid and/or fractionated local electrograms. Brown dots represent ablation points.

Figure 2  Complex fractionated atrial electrogram recordings and atrial fibrillation termination during complex fractionated atrial electrogram ablation. (A) Baseline complex fractionated atrial electrogram during ongoing atrial fibrillation. The tracings from top to bottom are surface electrocardiogram leads III and V1, local bipolar electrograms recorded with mapping/ablation catheter (MAP 1/2 and MAP 3/4), 14 bipolar electrograms recorded with the Orbiter catheter positioned in the left atrial appendage (Orbiter 1/2 to Orbiter 14/1), and 4 bipolar coronary sinus electrograms (CS 1/2 to CS 7/8). (B) Regularization of atrial fibrillation during radiofrequency ablation into an organized atrial tachycardia after complex fractionated atrial electrogram ablation between the left superior pulmonary vein and the left atrial appendage. Average cycle length was prolonged following ablation of some complex fractionated atrial electrograms. Tracings are as in (A). (C) Continuation of complex fractionated atrial electrogram ablations resulted in termination of atrial fibrillation to sinus rhythm. Tracings are as in (A).
two-tailed unpaired t-test, Mann–Whitney U test, or one-way ANOVA for continuous variables. A P-value of <0.05 was considered to indicate statistical significance.

Results

Baseline characteristics

Baseline characteristics of the patients are shown in Table 1. There were 60 men and 17 women with a mean age of 59.7 ± 10.2 years. History of AF ranged from 18 to 108 months (mean 74) with no difference between the groups: 73.1 months (range 17–108) in the CFAE group vs. 71 months (range 25–111) in the CFAE plus PVI group (P = 0.30). Median AF duration prior to ablation was 19 (4–24) months. Thirty-eight patients had evidence of structural heart disease: arterial hypertension (n = 23), valvular disease (n = 6), coronary artery disease (n = 5), and dilated cardiomyopathy (n = 4). The mean LA size was 48.6 ± 5.9 mm and the mean left ventricular shortening fraction was 30.6 ± 7.4%.

Procedural data

Procedural data are shown in Table 2. There were significant differences between the two groups with respect to procedure duration, number of RF current applications, fluoroscopy time, and number of patients in whom sinus rhythm or regularization was achieved.

Sinus rhythm at the end of the ablation procedure was achieved in 2 of 23 patients of the CFAE group and 15 of 54 patients of the CFAE plus PVI group (9 vs. 28%, P = 0.11). Pulmonary vein isolation was initially successful in 208 of 212 (98%) of all targeted PVs (waiting period of 30 min). In the CFAE plus PVI group, 4.9 ± 1.4 regions with CFAEs were ablated vs. 6.4 ± 1.6 in the CFAE group (P = 0.001). In the CFAE group, CFAEs were ablated in the region near the PVs in 21 of 23 patients. In the CFAE plus PVI group, CFAEs near the PVs were targeted after successful PVI in 35 of 54 patients. The anatomic regions of CFAE ablation are shown in Table 3.

Atrial fibrillation termination during ablation

Atrial fibrillation terminated during ablation in 44 of 77 patients (57%). Among these 44 patients, AF converted to sinus rhythm in 17 patients and to atrial flutter in 27 patients (Table 2 and Figure 2). In these 27 patients, atrial flutter circuits were pleomorphic. In the remaining 33 patients, AF was converted to sinus rhythm by trans-thoracic cardioversion at the end of the procedure.

In the CFAE group, AF terminated in nine patients (39%); in seven, AF regularized to atrial tachycardia and in two, it converted to stable sinus rhythm after regularization to atrial tachycardia. In 14 patients (61%), no acute effect of CFAE ablation was noted. In the CFAE plus PVI group, AF converted to sinus rhythm (15 of 54 patients; 28%) or organized into atrial tachycardia during CFAE ablation (20 of 54 patients; 37%). In the 15 patients with AF termination and conversion to sinus rhythm, AF stopped without prior organization in 3 patients and after regularization into atrial tachycardia in 12 patients. In 19 patients (35%), AF persisted after CFAE ablation.

Table 1 Clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CFAE group (n = 23)</th>
<th>CFAE + PVI group (n = 54)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.2 ± 8.7</td>
<td>56.6 ± 10.6</td>
<td>0.25</td>
</tr>
<tr>
<td>Male patients</td>
<td>17 (74%)</td>
<td>43 (80%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Duration of AF (months)</td>
<td>73.1 ± 48.5</td>
<td>71.0 ± 81.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Duration without interruption (months)</td>
<td>12.4 ± 9.2</td>
<td>21.4 ± 33.6</td>
<td>0.71</td>
</tr>
<tr>
<td>Unsuccessful anti-arrhythmic drugs</td>
<td>2.4 ± 0.9</td>
<td>2.4 ± 0.86</td>
<td>0.81</td>
</tr>
<tr>
<td>Amiodarone use (no.)</td>
<td>12 (55%)</td>
<td>19 (36%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (27%)</td>
<td>17 (32%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2 (9%)</td>
<td>3 (6%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Valvular cardiomyopathy</td>
<td>1 (5%)</td>
<td>5 (9%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>1 (5%)</td>
<td>3 (6%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Left ventricular fractional shortening (%)</td>
<td>33.1 ± 7.3</td>
<td>29.7 ± 7.7</td>
<td>0.05</td>
</tr>
<tr>
<td>LA parasternal diameter (mm)</td>
<td>46.9 ± 6.1</td>
<td>49.1 ± 5.6</td>
<td>0.12</td>
</tr>
<tr>
<td>RA parasternal diameter (mm)</td>
<td>58 ± 4.5</td>
<td>51.5 ± 6.9</td>
<td>0.02</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>49.7 ± 4.1</td>
<td>50.4 ± 5.7</td>
<td>0.71</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>33.0 ± 5.2</td>
<td>34.5 ± 7.4</td>
<td>0.36</td>
</tr>
<tr>
<td>Septum (mm)</td>
<td>12.1 ± 2.4</td>
<td>12.8 ± 2.9</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Data are means ± SD or number of patients (%). PVI, pulmonary vein isolation; CFAE, complex fractionated atrial electrogram; AF, atrial fibrillation; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; RA, right atrium.

Table 2 Procedural data

<table>
<thead>
<tr>
<th></th>
<th>CFAE group (n = 23)</th>
<th>CFAE + PVI group (n = 54)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure duration (min)</td>
<td>267 ± 113</td>
<td>332 ± 94</td>
<td>0.003</td>
</tr>
<tr>
<td>Radiofrequency applications (nr)</td>
<td>74.8 ± 29.2</td>
<td>102.4 ± 37.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Fluoroscopy duration (min)</td>
<td>49.2 ± 27.1</td>
<td>69 ± 25.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Fluoroscopy dosage (gcym²)</td>
<td>7803 ± 5570</td>
<td>8661 ± 7389</td>
<td>0.57</td>
</tr>
<tr>
<td>Sinus rhythm after CFAE ablation</td>
<td>2 (9%)</td>
<td>15 (27%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Sinus rhythm or regularization after CFAE ablation</td>
<td>9 (39%)</td>
<td>35 (65%)</td>
<td>0.034</td>
</tr>
</tbody>
</table>
Table 3: Anatomic regions of ablation of complex fractionated atrial electrograms

<table>
<thead>
<tr>
<th>Region</th>
<th>CFAE group (n = 23)</th>
<th>CFAE + PVI group (n = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septum including Bachman’s bundle region</td>
<td>21 (91%)</td>
<td>36 (67%)</td>
</tr>
<tr>
<td>Left postero-septal mitral annulus</td>
<td>21 (91%)</td>
<td>39 (72%)</td>
</tr>
<tr>
<td>Coronary sinus</td>
<td>19 (83%)</td>
<td>29 (54%)</td>
</tr>
<tr>
<td>Pulmonary veins</td>
<td>21 (91%)</td>
<td>35 (65%)</td>
</tr>
<tr>
<td>Roof of left atrium</td>
<td>13 (57%)</td>
<td>29 (54%)</td>
</tr>
<tr>
<td>Mitral annulus</td>
<td>17 (74%)</td>
<td>39 (72%)</td>
</tr>
<tr>
<td>Right atrial cavotricuspid isthmus</td>
<td>5 (22%)</td>
<td>12 (22%)</td>
</tr>
<tr>
<td>Crista terminalis</td>
<td>9 (39%)</td>
<td>10 (19%)</td>
</tr>
<tr>
<td>Left atrial appendage</td>
<td>19 (83%)</td>
<td>38 (70%)</td>
</tr>
<tr>
<td>Number of ablation sites/ patient</td>
<td>4.9 ± 1.4</td>
<td>6.3 ± 1.6</td>
</tr>
</tbody>
</table>

Long-term outcome after a single ablation

After a mean follow-up time of 13 ± 10 months, sinus rhythm was present in the absence of anti-arrhythmic drug therapy after a single ablation procedure in 2 of 23 patients (9%) undergoing CFAE ablation compared with 22 of 54 patients (41%) undergoing CFAE plus PVI ablation (P = 0.008).

Long-term outcome after repeat ablation procedures

After repeat ablation procedures, sinus rhythm was present without anti-arrhythmic drugs at the end of follow-up in 39 of 54 patients (72%) undergoing CFAE plus PVI. This was achieved by a single ablation procedure in 22 of 39 patients and a repeat ablation procedure in 17 patients. In the CFAE group, sinus rhythm without anti-arrhythmic drug therapy was achieved in 5 of 23 patients (22%; P < 0.001 compared with CFAE plus PVI group) with three patients undergoing a repeat ablation procedure.

Complications

No procedure-related complications were observed. No patient had PV stenosis acutely or during follow-up (MRI or CT evaluation).

Discussion

Main finding

The main finding of this study is that RF ablation of CFAEs used as a stand-alone ablation strategy results in maintenance of sinus rhythm in only 9% of patients with persistent AF during a follow-up period of 13 ± 10 months compared with a success rate of 41% in patients treated by a combined CFAE ablation plus PVI strategy. After repeat ablation procedures, sinus rhythm was maintained in 22% of patients undergoing CFAE ablation as a stand-alone strategy and in 77% of patients undergoing CFAE plus PVI ablation approach.

The efficacy of CFAE ablation as a stand-alone strategy in our study is lower than that reported in the study by Nademanee et al. Several factors may explain the difference in results between these studies: First, based on the mean LA size (42 ± 6 in the study by Nademanee et al. vs. 48.6 ± 5.9 mm in our study), our study included patients with more diseased atria, a factor that may have predisposed for lower acute and long-term success rates. Secondly, we performed the ablation lesions with a 4 mm irrigated-tip catheter with moderate power settings (maximal 30–35 W), whereas Nademanee et al. used higher power settings (70–80 W). By using higher power settings, larger lesions including larger areas with CFAE might have been created. Thirdly, we applied more stringent criteria for follow-up after the ablation procedure, including repeated 7-day Holter recordings, which may have resulted in a better detection of the AC recurrences.

The concept of complex fractionated atrial electrogram ablation

In a landmark work, Konings et al. described high-density mapping of electrically induced AF in patients with Wolff–Parkinson–White syndrome undergoing surgery using a spoon-shaped electrode with 244 unipolar electrodes. In that study, the right atrium was investigated and was found to be activated by one or multiple wavelets propagating in different directions. The authors demonstrated that distinct electrophysiological properties, such as slow conduction, functional conduction block, and pivot points, were associated with the occurrence of complex fractionated local electrograms. Morillo et al. demonstrated in a model of induced AF in dogs that cryo-ablation at the sites of the shortest AF CL led to termination and non-inducibility of AF. Based on these findings, Nademanee et al. described a new approach for catheter ablation of AF targeting local CFAEs or local electrograms with a very short CL without attempting to isolate the PVs. The authors hypothesized that local fractionated or high-frequency electrograms indicate the electrophysiological substrate supposed to maintain AF. In their study, the ablation of CFAE areas resulted in termination of AF in 91% of patients, and 77% remained free of symptomatic AF at 1-year follow-up. These encouraging results supported the idea that areas with CFAEs are critical for AF perpetuation and may serve as ablation target sites.

Complex fractionated atrial electrogram ablation and pulmonary vein isolation

A recent study by Oral et al. showed that RF ablation of LA and CS CFAEs without PVI has a success rate of 33% in patients with chronic AF. To achieve a success rate of 57%, repeat ablation procedures were necessary in 44% of patients. Interestingly, in this study, tachycardias arising from the PV were found in all patients during repeat ablation procedures. These results suggest that PVI during the initial ablation session would have protected against recurrent arrhythmias. This finding supports the opinion that PVs are not only responsible for triggering AF, but also may be critical in the occurrence and maintenance of atrial tachyarrhythmias following AF ablation.

Our study supports the relevance of the PVI in addition to CFAE ablation in patients with persistent AF. In the present study, the single procedure success rate improved from 9% for stand-alone CFAE ablation to 41% for CFAE ablation.
with PVI. A recent study from our group showed that the success rate for this combined approach improved from 41% with a single ablation procedure to 74% with further ablation procedures. As shown in a recent study by Porter et al., CFAE ablation appears to be promising, especially in combination with other ablation techniques such as PVI. The reasons for the beneficial effect of additional PVI are not entirely known. The ostial and peri-ostial regions of the PVs might have been targeted less extensively during CFAE ablation than during CFAE ablation plus PVI approach. Presumably, localized (micro-)re-entries at the PV ostia serving as a substrate for AF maintenance may require the more proximal parts of PVs for re-entry perpetuation. If the more proximal part of the PV is disconnected by complete ostial PVI and no longer participates in the hypothetical re-entrant circuits, then re-entrant rhythms cannot arise or persist.

Complex fractionated atrial electrogram ablation analysis

In the present study, CFAEs were identified using automated signal analysis algorithms in only a subset of patients. In a recent study, we showed that by visual inspection of electrogram morphology, ablation of CFAE was feasible and resulted in AF termination in ~30% or organization of in ~50% of patients with persistent AF. However, identification of the regions with CFAE that may serve as ablation targets is dependent on the operator’s judgement. Recently, Scherr et al. described an automated detection and characterization of CFAEs in human LA using AF using a software for automated detection (CFAE Software Module, CARTO XP System). The study demonstrated the feasibility of detection and characterization of CFAEs using new software algorithms. In persistent AF, CFAE were distributed evenly all over the LA with only small differences in CFAE density in the different LA regions. In line with these findings, we did not identify specific atrial regions that showed higher density of CFAE when compared with other regions. Using a different automated software algorithm, Verma et al. demonstrated that CFAE ablation resulted in AF CL prolongation, regularization, and non-inducibility in most patients with paroxysmal or persistent AF. Using an automated mapping algorithm (CARTO XP), we also found a ubiquitous CFAE distribution in persistent AF. A recent prospective study showed that various patterns of complex electrograms were ubiquitously distributed in the LA and CS regions in patients with chronic AF. The study showed that the percentage of continuous activity and a temporal gradient of activation at the ablation areas were associated with slowing or termination of AF, independent of the region. This suggests that distribution of CFAE in persistent AF might be highly variable and CFAE ablation cannot be guided by uniform anatomically based criteria.

Post-ablation tachyarrhythmias

Most tachyarrhythmia relapses during follow-up were due to recurrent AF (77%). Nevertheless, macro-re-entrant atrial flutter occurred in a sizeable percentage of patients and often multiple re-entrant circuits were identified. Theoretically, this type of arrhythmia might be expected to be less common following CFAE ablation than after ablation procedures involving linear lesions. With the circumferential and/or linear ablation approach, non-contiguous ablation lesions can be avoided. The ablation of areas with CFAE might favour creation of slow conduction zones that may facilitate the occurrence of stable micro-re-entrant or macro-re-entrant rhythms. It has been described that non-contiguous ablation lesions may lead to narrow isthmuses of slow conduction and LA re-entry after ablation of AF. Nademanee et al. described patients who developed atypical atrial flutter with the re-entrant circuits clearly defined close to the areas of previous RF current applications.

Limitations of the study

We recognize that the current study has some limitations. Although patients’ characteristics were balanced between groups undergoing different ablation strategies, the current study represents a retrospective analysis of non-randomized patients. Automated signal analysis algorithms were used in only 40% of the patients. However, visual identification of CFAE by experienced operators is considered a gold standard for verification of the accuracy of the automated detection algorithms. Although it is recognized that visual identification of CFAEs is difficult and dependent on the operator’s experience, operators who performed ablation procedures in our study have more than 5 years of experience in AF ablation. Furthermore, we found no differences in ablation efficacy with regard to the use of automated algorithms. Finally, we used a power limit of 35 W with an open irrigated-tip ablation catheter, whereas other groups report RF energy application with an 8 mm tip and a power up to 70 W.

Conclusion

Complex fractionated atrial electrogram ablation as a stand-alone ablation strategy is associated with a low success rate during a mid-term follow-up and therefore seems to be insufficient as a sole ablation strategy for patients with persistent AF. This ablation in combination with PVI increases the success rate of a single ablation procedure in these patients. These findings support the consideration of PVI as a part of an ablation approach in patients with persistent AF regardless of the CFAE location.

Conflict of interest: none declared.

References


