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Original Article

The optimal setting of complex fractionated atrial electrogram software in substrate ablation for atrial fibrillation

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ABSTRACT

Background: Complex fractionated atrial electrogram (CFAE)-targeted catheter ablation (CFAE ablation) requires a high rate of atrial fibrillation (AF) termination to provide good outcomes. We determined the optimal settings of CFAE software.

Methods: In our 430 consecutive patients, AF was terminated in 97 (234/242) and 79% (149/188) of patients with paroxysmal and persistent AF, respectively, by CFAE ablation combined with (31%) or without (69%) pulmonary vein isolation, occasionally with nifekalant infusion. We analyzed 109 consecutive patients who underwent CFAE ablation to determine the optimal settings for comparing subjective versus objective decisions by the CFAE software on CARTO3. We compared three settings: the default setting (0.05–0.15 mV, 50–120 ms) and two modified settings (#1: 0.05–0.30 mV, 40–70 ms, #2: 0.05–0.13 mV, 10–20 ms). We retrospectively analyzed 11,425 points during left atrial mapping before ablation and 10,306 points that were subjectively detected and ablated as CFAE points. An interval confidence level ≥ 6 denoted a site with CFAE.

Results: With the default setting, the accuracy, sensitivity, specificity, positive productive value, and negative productive values were 67, 42, 77, 48, and 73%, respectively. With modified setting #1, the values were 78, 55, 87, 74, and 77%, respectively, versus 64, 82, 60, 53, and 91%, respectively, for modified setting #2.

Conclusion: These data suggest that setting #1 was generally superior to the default setting, whereas setting #2 was optimal for excluding areas not requiring ablation. The optimal CFAE software setting was a voltage of 0.05–0.30 mV and an interval parameter of 40–70 ms.

1. Introduction

Catheter ablation is an effective approach for the management of patients with atrial fibrillation (AF) [1–7]. Pulmonary vein isolation (PVI) is one of the most common strategies of AF ablation, but the outcome of PVI alone for patients with persistent AF is poor [8–10]. Additional approaches such as linear ablation after PVI have been reported to improve the outcome [11–15]. Nademanee et al. also described an alternative approach for AF ablation that involved identifying the target "substrate" sites via electroanatomical mapping of complex fractionated atrial electrograms (CFAEs) [7–16,17]. Although PVI was not required with this approach, AF ablation guided by CFAEs resulted in a high rate of success in maintaining sinus rhythm in patients with either paroxysmal or persistent AF. However, the results of these studies were not replicated by others [6,18,19]. Thus, the role of CFAE-targeted catheter ablation (CFAE ablation) in treating patients with AF remains controversial. Because one of our physicians was a fellow at the Pacific Rim Electrophysiology Research Institute, all five physicians in our Institute similarly terminate AF with CFAE ablation [20,21]. In our latest study of 430 consecutive patients, AF was terminated by CFAE ablation with ($n=133$) or without ($n=297$) PVI in 97 (234/242) and 79% (149/188) of patients with paroxysmal and persistent AF, respectively, occasionally with nifekalant infusion without cardioversion. Thus, the use of optimal CFAE software

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settings on the CARTO3 may help physicians detect CFAE areas. Therefore, we determined the optimal setting of CFAE software on the CARTO3 system.

2. Materials and methods

2.1. Study population and protocol

This study comprised 109 consecutive patients (22 females, 87 males; mean age of 59 ± 10 years), including 57 (52%) patients with paroxysmal AF, 40 (37%) patients with persistent AF, and 12 (11%) patients with long-standing persistent AF with symptomatic drug refractory AF, who successfully underwent CFAE ablation combined with (n=44) or without (n=65) PVI between May 2011 and May 2012. Thirty-seven patients had histories of AF ablation. The patient characteristics and procedure data are shown in Tables 1 and 2, respectively.

All antiarrhythmic drugs were discontinued at least five half-lives before ablation, excluding amiodarone, which was discontinued at least 3 months before ablation. Warfarin was not discontinued, and all patients provided written informed consent for the procedure. This study protocol was approved by our institutional ethics committee (Approval date: July 18, 2013, Approval number: 355). AF was defined in accordance with the 2007 Heart Rhythm Society Expert Consensus Statement [22]. Paroxysmal AF was defined as recurrent AF (≥ 2 episodes) that terminates spontaneously within 7 days. Persistent AF was defined as AF that is sustained for > 7 days or AF lasting < 7 days but necessitating pharmacologic or electrical cardioversion. AF lasting > 1 year was defined as longstanding persistent AF.

Table 1
Patient characteristics.

	Paroxysmal AF (n=57)	Persistent AF (n=40)	Longstanding persistent AF (n=12)
Age (years)	59 ± 11	58 ± 9	60 ± 7
Male (%)	77	85	75
Body mass index (kg/m^2)	24.7 ± 3.0	25.1 ± 4.2	27.3 ± 3.5
Hypertension (%)	56	53	67
Diabetes mellitus (%)	11	20	25
Heart failure (%)	14	25	25
HHD (%)	18	33	17
DCM (%)	4	8	0
HCM (%)	2	13	0
Ischemic heart disease (%)	7	8	0
Post cardiac operation (%)	4	3	0
Left atrial diameter (mm)	39.8 ± 6.0	46.7 ± 6.2	51.7 ± 5.0
Left atrial volume (ml)	61.3 ± 19.9	82.7 ± 24.9	99.5 ± 29.9
LVEF (%)	65.0 ± 12.1	59.4 ± 13.1	65.7 ± 6.5
BNP (pg/ml)	98.6 ± 175.2	177.9 ± 129.2	113.5 ± 79.4
ANP (pg/ml)	120.2 ± 528.1	74.6 ± 43.9	57.0 ± 27.5

HHD, hypertensive heart disease; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; AF, atrial fibrillation.

Table 2
Procedure data.

	Paroxysmal AF (n=57)	Persistent AF (n=40)	Longstanding persistent AF (n=12)
CFAE ablation combined with PVI (%)	56	48	33
Procedure time (min)	222 ± 45	229 ± 46	257 ± 47
Radiofrequency duration (min)	85 ± 24	87 ± 20	114 ± 20
Fluoroscopic time (min)	16 ± 10	14 ± 10	10 ± 7
Mapping points before ablation	105 ± 30	109 ± 48	124 ± 27
Mapping duration (min)	5 ± 2	6 ± 2	5 ± 1
Use of cardioversion (%)	5	10	33
Use of nifekalant (%)	49	70	92

Mapping site/time; needed site/time for creating an electroanatomical map.
AF, atrial fibrillation; CFAE, complex fractionated atrial electrogram; PVI, pulmonary vein isolation.

2.2. Mapping and ablation of AF

The AF ablation technique described by Nademanee et al. [7,16,17] was used for this study, as previously reported [20,21,23,24]. In brief, a 3.5-mm NaviStar ThermoCool catheter (DF or FJ curve; Biosense Webster, Diamond Bar, CA, USA) was used in all cases. After the coronary sinus (CS) was cannulated via the femoral vein using a decapolar catheter (Dynamic XT Decapolar Steerable-Cath; C. R. Bard, Murray Hill, NJ, USA) for recording and induction, patients underwent non-fluoroscopic electroanatomical mapping with CARTO3 (Biosense Webster). Heparin (3000 IU initial bolus, 1000–2000 IU subsequent boluses as needed to maintain the activated clotting time > 300 s) was administered for anticoagulation.

All electroanatomical maps were created for patients who displayed AF, either occurring spontaneously or by induction. Burst pacing using a CS catheter to a lower limit of 1:1 capture or up to 150 ms was used to induce AF occasionally with a 0.01–0.02 μg/kg/min isoproterenol infusion. AF was inducible in all patients at the beginning of the procedure. When AF was terminated during ablation procedure in patients with paroxysmal AF, AF was re-induced until it was no longer inducible, as paroxysmal AF could be terminated spontaneously. Electroanatomical maps were created and displayed as a shortest complex interval (SCI) map, and the areas of CFAE were also identified manually, tagged, and associated with the atrial anatomy created by CARTO3. This enabled the operators to associate areas of CFAE with the left atrium (LA), CS, and occasionally the right atrium, thereby identifying target sites for ablation.

Bipolar recordings were filtered at 30–500 Hz, and the CFAEs were defined as follows: (1) fractionated electrograms composed of two or more deflections and/or a perturbation of the baseline with continuous deflection of a prolonged activation complex; and (2) atrial electrograms with an extremely short cycle length (≤ 120 ms). Examples of two intracardiac electrocardiograms displaying CFAEs and normal atrial electrograms are shown in Fig. 1. Typical continuous CFAEs before radiofrequency (RF) applications are easy to detect, but the electrograms look different in each case and each state of ablation. When AF is organized, CFAEs are also organized. After a certain amount of RF applications, the amplitude and frequency were decreased. This may be one of the reasons that CFAE ablation has not been replicated easily by others [6]. We use CFAE software but subjectively determine which electrograms are CFAEs. All of the operators in our institute replicate CFAE ablation. Then, we tried to optimize the CFAE software to perform CFAE ablation clinically in other institutes with our subjective decision. Then, the CFAE sites in this study were defined as those that we ablated. In addition, we calculated what setting is most appropriate to match our subjective decisions.

After acquiring the SCI map associated with CFAEs, we searched the areas of CFAEs referring to the tagged points because CFAE areas have temporal spatial stability. RF was delivered with a maximal power of 40 W with irrigation rates of 30 mL/min (3.5-mm NaviStar ThermoCool catheter; Biosense Webster). The power was reduced to 15 W in the posterior LA close to the esophagus or in the CS. The primary endpoints during RF ablation were either complete elimination of CFAE areas or conversion of AF to sinus rhythm occasionally with the injection of nifekalant (0.3 mg/kg intravenously over 10 min, maximum twice), a Class III antiarrhythmic drug similar to ibutilide, which is not available in Japan. If the atrial arrhythmias were not successfully terminated, then internal cardioversion was performed. The endpoints of the procedure were termination of AF in patients with persistent AF