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Original article

The efficacy of ablation based on the combined use of the dominant frequency and complex fractionated atrial electrograms for non-paroxysmal atrial fibrillation

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ABSTRACT

Background: This study aimed to evaluate an approach for an endpoint of non-inducibility using a combined high-dominant frequency (DF) and continuous complex fractionated atrial electrogram (CFAE) ablation following circumferential pulmonary vein isolation (PVI) in a sequential fashion, including linear ablation as compared to PVI alone.

Methods and results: A total of 84 non-paroxysmal patients with atrial fibrillation (AF) were investigated retrospectively. The AF patients were divided into two groups: patients with PVI following a combined high-DF and continuous CFAE ablation with linear ablation (substrate modification group, $n = 59$) and those with PVI alone ($n = 25$). DF sites of $\geq$8 Hz and then continuous CFAE sites defined by fractionation intervals of $\leq$50 ms were modified after PVI. The ablation endpoint was non-inducibility. Atrial tachyarrhythmias (ATs) could not be induced in 54 of 59 (92%) patients after a sequential ablation, and in 18 of 25 (64%) with PVI alone. The ATs freedom without antiarrhythmic drugs in the substrate modification group was significantly greater than that in those with PVI alone after 1 procedure during 12 months of follow-up (78.6% vs. 53.8%, log-rank test $p = 0.039$).

Conclusion: This sequential approach using a substrate based ablation was associated with a better clinical long-term outcome as compared to PVI alone.

Introduction

Pulmonary vein isolation (PVI) has become an accepted treatment for atrial fibrillation (AF) [1], and atrial substrate modification using complex fractionated atrial electrogram (CFAE) and linear ablation are considered necessary in patients with non-paroxysmal atrial fibrillation (NPAF) [2,3]. However, these strategies for an endpoint of AF termination may produce occurrences of post-ablation atrial tachyarrhythmias (ATs) [4]. ATs occur in up to 50% of patients following extensive ablation of persistent AF [5]. Although the mechanisms sustaining AF have not been fully identified, localized electrical sources are reported to be prevalent sustaining mechanisms of human AF using specific computational mapping devices [6]. On the other hand, high-dominant frequency (DF) [7,8] and continuous CFAE sites defined by average fractionated intervals (FIs) of $\leq$50 ms [9,10] as a surrogate for localized sources maintaining AF are also potential AF ablation targets. In a previous report, a combined high-DF and continuous CFAE site ablation after circumferential PVI was effective in maintaining sinus rhythm (SR) in paroxysmal and persistent AF patients [11]. By limiting the extent of RF applications to the atria, this strategy may help limit occurrences of post-ablation ATs that follow a more aggressive ablation. However, the strategy has not been fully evaluated as compared to PVI alone. In this study, AF inducibility, not AF termination, as an endpoint after each step in the step-wise NPAF ablation process was introduced. Therefore, this study aimed to evaluate an ablation approach for an endpoint of non-inducibility using a combined high-DF and continuous CFAE site ablation following PVI in a step-wise fashion, including linear ablation as compared to PVI alone.

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Methods

Study population

A total of 84 NPAF patients between January 2011 and September 2012 were investigated retrospectively. The patients that underwent PVI and substrate modification included 29 (49%) with persistent AF (duration 7.3 ± 3.5 months, range 2–12 months) and 30 (51%) with long-standing persistent AF (duration of 45 ± 26 months, range 14–120 months) (Table 1). The patients that underwent PVI alone included 12 (48%) with persistent AF (duration 6.5 ± 3.3 months, range 3–12 months) and 13 (52%) with long-standing persistent AF (duration of 23 ± 10 months, range 13–44 months). Persistent AF was defined as AF lasting ≥7 days but <1 year, and long-standing AF as continuous AF lasting ≥1 year [12].

Electrophysiological study

The protocol was approved by the Institution Research and Ethics Committee. All patients gave their documented informed consent before the ablation procedure. All antiarrhythmic drugs (AADs) were discontinued for at least 5 half-lives. The electrophysiological study and ablation procedure have been previously described [11]. In brief, a 5-french deflectable catheter was inserted into the coronary sinus (CS) via the right femoral vein. The transseptal procedure was performed using fluoroscopic landmarks and three 8 F SL0 sheaths (St. Jude Medical, Inc., St. Paul, MN, USA) were advanced into the left atrium (LA). After the transseptal procedure, a single bolus of 5000 U of heparin was administered. Heparinized saline was continuously infused to maintain an activated clotting time of 300–350 s. After creating a 3D biatrial geometry using a NavX system (NavX, with CFE software, St. Jude Medical Inc.), a 7 F decapolar circular catheter (Lasso, Biosense-Webster, Inc., Diamond Bar, CA, USA) was used for sequential contact mapping.

Signal recording and analysis

The points in each region were similar in number and nearly equally distributed to avoid a too-high density [LA: 165 ± 33 points, right atrium (RA): 140 ± 41 points] [10–13]. The mapping parameter (CFAE-mean) was defined as an interval-analysis algorithm that measured the average index of the fractionation. Recordings at each site were 5 s in length [10]. A continuous CFAE was defined by an average FI of ≤50 ms, indicating a high degree of temporal stability of the fractionated electrograms maintaining AF [10,14]. The fast Fourier transform (FFT) method has been described previously. Signals were truncated to 3.41 s at sampling rates of 1200 Hz, providing 4096 points for analysis (resolution 0.29 Hz). The signals were rectified and processed by a Hanning window function and filtered from 2 to 100 Hz. The point DF was determined as the frequency associated with the maximum peak power of the spectrum. Only DF points with an FFT ratio >0.2 were included [7,15]. The high-DF site cut-off value was set at 8 Hz according to previous studies [15].

Table 1
Clinical characteristics.

	PVI + substrate modification (N = 59)	PVI alone (n = 25)	p-Value
Age (years)	64 ± 9.0	55 ± 12	0.001
Male (%)	46 (78%)	22 (88%)	0.173
Long-standing AF (%)	30 (51%)	13 (52%)	0.923
Duration of AF (months)	26 ± 27	15 ± 12	0.211
CHA2DS2-VASc	1.8 ± 1.4	0.8 ± 1.2	0.001
0 or 1	27	19	0.011
2 or more	32	6	0.011
Diabetes	8	0	–
Hypertension	32 (54%)	8 (32%)	0.064
LA diameter (mm)	44 ± 7	45 ± 5	0.121
LVEF (%)	58 ± 10	57 ± 13	0.581
Number of failed AADs	0.7 ± 0.7	1.0 ± 0.8	0.123

AADs, antiarrhythmic drugs; AF, atrial fibrillation; LA, left atrium; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation.

Sequential ablation approach

The ablation procedure was performed using a sequential ablation approach consisting of PVI as a first step followed by a high-DF and continuous CFAE site ablation as a second step and linear ablation as the final step. When AF organized to atrial tachycardia (AT), activation mapping and ablation were performed. The endpoint of ablation was non-inducibility.

The PVI was performed guided by two 7-F decapolar circular catheters positioned at the ipsilateral PV ostia [11]. Each radiofrequency (RF) energy application was delivered for 40 s. A 3.5-mm irrigated tip RF catheter (Safire, St. Jude Medical Inc.) was used with the temperature limited to 42 °C and power to 30 W (with a flow rate of 13 mL/min). A maximum power of ≤25 W was used while delivering energy to sites near the esophagus. After the elimination or dissociation of the PV potentials, exit block was confirmed by pacing from circular catheters placed within the PVs.

After the PVI, fractionation and frequency analyses were performed as mentioned above. All high-DF sites in the LA, RA, and inside the CS were targeted for ablation, starting with the highest DF points. Ablation at a DF site was continued for 40–60 s until the local electrograms were eliminated. A maximum power of ≤25 W was used while delivering energy inside the CS. After the high-DF site ablation, the continuous CFAE sites were ablated, starting with the shortest FI points. The continuous CFAE site ablation was performed in the same manner as the high-DF site ablation. When AF continued despite targeting all high-DF and continuous CFAE sites after the PVI, external cardioversion was performed.

LA linear ablation consisting of a roof, inferior mitral annulus, or mitral isthmus lines was performed in this study as the final step when the ATs were induced after second step [2,4]. When ATs continued despite linear ablation, external cardioversion was performed. The procedure was completed with a cavotricuspid isthmus (CTI) ablation in all patients who regained SR. When the induced ATs continued for at least 2 min, external cardioversion was performed [16].

Induction protocol

After recovering SR, the AT's inducibility was evaluated by a modest stimulation protocol to limit occurrences of post-ablation ATs that follow a more aggressive ablation. Bursts of 10 beats were delivered starting at a cycle length of 250 ms and pacing output of 10 mA and 2 ms pulse width. The 10-beat bursts were repeated with 10 ms decrements for each subsequent burst until 2:1 atrial capture or a minimum cycle length of 190 ms. The stimulation protocol consisting of one induction attempt was performed from the LA using bipolar electrodes in the distal CS without an isoproterenol injection. Induced ATs were defined as those sustained for at least 2 min [16].

Post-procedure care and follow-up

A clinical interview, surface electrocardiogram, and 24-h Holter monitoring were performed 1 day after the procedure and repeated 1, 3, 6, 9, and 12 months after the catheter ablation.