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Original Article

Efficacy of atrial substrate modification based on dominant frequency of paroxysmal atrial fibrillation

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ABSTRACT

Background: The endpoint of ablation procedures is suggested to be non-inducibility of paroxysmal atrial fibrillation (PAF). However, the prognosis of induced AF/atrial tachycardia (AT) after pulmonary vein isolation (PVI) in PAF patients remains unclear.

Methods: A total of 122 PAF patients were divided into the following 3 groups: Group 1, 79 without AF/AT induced after PVI; Group 2, 21 with AF/AT induced or sustained after PVI, and followed by a high-dominant frequency (DF) and continuous complex fractionated atrial electrogram (CFAE) site ablation and, if necessary, linear ablation; and Group 3, 22 with external cardioversion of AF/AT induced or sustained after PVI. High-DF (DF $\geq$ 8 Hz) and continuous CFAE (fractionated intervals $\leq$ 50 ms) sites were targeted. The ablation endpoint was non-inducibility of PAF.

Results: In Group 2, AF terminated in 2 patients with a high-DF and continuous CFAE site ablation. In 4 patients, AF induced after cardioversion did not terminate with left atrium linear ablation, and required additional cardioversion. Common atrial flutter in 2 patients terminated with cavotricuspid isthmus ablation. An AT terminated with a roofline ablation. Finally, no AF/AT could be induced in any of the patients in Group 2 after all the procedures. The cumulative freedom from AF/AT recurrence without antiarrhythmic drugs in Groups 1 and 2 was significantly greater than that in Group 3 after 1 procedure during 12 months of follow-up (90% and 91% vs. 64%, Log-rank test $P=0.001$ and $P=0.033$, respectively).

Conclusions: Atrial substrate ablation may improve the clinical outcome after ablation in patients after PVI with residual arrhythmia inducibility.

1. Introduction

Catheter ablation is an effective therapy for atrial fibrillation (AF). Pulmonary vein isolation (PVI) has become an accepted treatment for AF [1]. Atrial substrate modification is considered necessary in patients with non-paroxysmal AF (NPAF) rather than paroxysmal AF (PAF) [2,3]. The endpoint of the ablation procedure has been suggested to be the non-inducibility of PAF. For PAF, an additional ablation of non-PV AF triggers is considered necessary in addition to the PVI. However, prior reports showed AF recurrence rates of 19–33% in the non-induced group and 36–55% in the induced group [4–6]. The diagnostic accuracy of AF induction tests after ablation seems to be low for predicting AF recurrences. Therefore, the need for further ablation of the induced atrial arrhythmias after the PVI in PAF patients remains unclear.

The efficacy of PVI is sometimes insufficient, and atrial substrate modification of target specific AF signals indicating the substrate responsible for AF perpetuation has been proposed [7,8]. Complex fractionated atrial electrograms (CFAEs), which are electrograms that show continuous fractionation and very short cycle lengths during AF, may represent the substrate of AF [7]. In addition, atrial sites that represent local electrograms with high dominant frequencies (DFs) may be associated with AF maintenance [8]. A recent study reported that high-DF sites and continuous CFAE sites as the atrial substrate following PVI were present even in paroxysmal AF [8]. Accordingly, the present study aimed to evaluate the need of such an atrial substrate modification for the induced atrial arrhythmias after circumferential PVI to guide the non-inducibility in PAF patients.

2. Materials and methods

2.1. Study population

A total of 122 consecutive AF patients with PAF (64 $\pm$ 9.3 years) between March 2011 and October 2012 were examined in a

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retrospective review. The protocol was approved by the research and ethics committee of Gunma Prefectural Cardiovascular Center on June 15, 2012. All patients provided written informed consent. The AF duration was 35 ± 47 months (range, 2–240). Paroxysmal AF was defined as AF lasting < 7 days [9]. All antiarrhythmic drugs (AADs) except oral amiodarone administered in 2 patients were discontinued for at least 5 half-lives, and no patients received any oral amiodarone therapy before the electrophysiological study.

2.2. Fractionation and frequency analysis

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 [8,10,11]. A continuous CFAE was defined by an average fractionated interval (FI) of ≤ 50 ms, indicating a high degree of temporal stability of the fractionated electrograms maintaining AF [11,12]. The fast Fourier transform (FFT) method has been described previously [12]. 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 a fast Fourier transform ratio > 0.2 were included [13,14]. The high-DF sites were defined as DFs of ≥ 8 Hz [14].

2.3. Ablation procedure

A NavX system (NavX with CFE software, St. Jude Medical Inc., St. Paul, MN, USA) was used for catheter ablation. A 5-french deflectable catheter was inserted into the coronary sinus (CS) via the right femoral vein. The trans-septal procedure was performed using fluoroscopic landmarks, and three 8-F SL0 sheaths (St. Jude Medical Inc.) were advanced into the left atrium (LA). After the trans-septal procedure, a single bolus of 5000 U of heparin was administered. A continuous infusion with heparinized saline was administered to maintain an activated clotting time of 300–350 s. The three-dimensional biatrial geometry was created on the NavX system, and sequential contact mapping was performed using a 7-F decapolar circular catheter (Lasso, Biosense-Webster Inc., Diamond Bar, CA, USA). The points in each region were similar in number and nearly equally distributed.

The ablation procedure was performed using an approach consisting of PVI followed by high-DF and continuous CFAE site ablation and, if necessary, linear ablation. When AF organized into AT, activation mapping and ablation were performed. The endpoint of the ablation was non-inducibility. The PVI was performed guided by two 7-F decapolar circular catheters (Lasso, Biosense-Webster Inc.) positioned at the ipsilateral PV ostia. At the anterior aspect of the left PVs, an ablation line was created along the ridge between the left atrial appendage (LAA) and PV ostium. 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 of 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 for continuous AF or induced AF as mentioned previously [8,15]. All high-DF sites in the LA, right atrium (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 fractionated interval points. The continuous CFAE site ablation was performed in the same manner as the high-DF site ablation.

When AF continued despite a high-DF and continuous CFAE site ablation, external cardioversion and induction were performed. For the induced AF, an LA linear ablation consisting of a roof line, inferior mitral annulus line, or mitral isthmus line was performed. When AF continued despite a linear ablation, external cardioversion and induction were performed. The procedure was completed with a cavotricuspid isthmus ablation in all patients who regained sinus rhythm. Finally, we tried to provoke PV reconnections by administering 10-mg intravenous injection of intravenous adenosine triphosphate (ATP) administered during an intravenous isoproterenol infusion (5 μg/min). Additional RF applications were performed to eliminate any ATP-reconnections.

2.4. Induction protocol

The atrial tachyarrhythmia inducibility was evaluated by a stimulation protocol as mentioned previously [15]. Bursts of 10 beats were delivered starting at a cycle length (CL) of 250 ms at a 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 CL 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 AF/AT was defined as that sustained for at least 2 min [16].

2.5. Post-procedure care and follow-up

A surface electrocardiogram (ECG) and 24-h Holter monitoring were obtained 1 day after the procedure and repeated 1, 3, 6, 8, 10, and 12 months thereafter by the referring cardiologist in our hospital as mentioned previously [15]. Antiarrhythmic medications were continued for at least 3 months to prevent any early recurrences of AF unless AF continued. When the patients had any clinical symptomatic palpitations after the AF ablation, examinations including an ECG, 24-h Holter monitoring, and assessment of the current condition were also performed on an outpatient basis. AF recurrence was defined as sustained AF lasting more than 30 s and confirmed by ECGs 3 months after the ablation [16]. A repeat ablation procedure was performed if AF recurred or there was an AT lasting more than 30 s. Procedural success was defined as a lack of AF or AT beyond 3 months post-ablation [9].

2.6. Statistical analysis

Continuous data are expressed as means ± SDs. Categorical variables are expressed as numbers and percentages. If the data showed a normal distribution, one-way analysis of variance was performed to identify statistically significant differences between the 3 groups. If the data did not have a normal distribution, the Kruskal–Wallis *H*-test was used. A Bonferroni post hoc test was used to compare the different groups. A Kaplan–Meier event-free survival analysis was conducted to assess the cumulative freedom from AF recurrence. Time-to-event analyses were performed using the Log-rank test. A *P* value of less than 0.05 was considered statistically significant.