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Original Article

Complex fractionated atrial electrograms, high dominant frequency regions, and left atrial voltages during sinus rhythm and atrial fibrillation

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ABSTRACT

Background: Ablation targeting complex fractionated atrial electrograms (CFAEs) or high dominant frequency (DF) sites is generally effective for persistent atrial fibrillation (AF). CFAEs and/or high DF sites may exist in low-voltage regions, which theoretically represent abnormal substrates. However, whether CFAEs or high DF sites reflect low voltage substrates during sinus rhythm (SR) is unknown.
Methods: Sixteen patients with AF (8 with paroxysmal AF; 8, persistent AF) underwent high-density mapping of the left atrium (LA) with a 3-dimensional electroanatomic mapping system before ablation. The LA was divided into 7 segments and the mean bipolar voltage recorded during AF and SR, CFAEs (cycle lengths of 50–120 ms), and DF sites were assessed in each segment with either a duo-decapolar ring catheter ($n=10$) or a 64-pole basket catheter ($n=6$). Low-voltage areas were defined as those of <0.5 mV during AF and <1.0 mV during SR.
Results: Regional mean voltage recorded from the basket catheter showed good correlation between AF and SR ($r=0.60$, $p<0.01$); however, the % low-voltage area in the LA recorded from the ring catheter showed weak correlation ($r=0.34$, $p=0.05$). Mean voltage was lower during AF than during SR (1.0 mV [IQR, 0.5–1.4] vs. 2.6 mV [IQR, 1.8–3.6], $p<0.01$). The regional and overall % low-voltage area of the LA was greater during AF than during SR (20% vs. 11%, $p=0.05$). CFAEs and high DF sites (>8 Hz) did not correlate with % low-voltage sites during SR; however, CFAEs sites were located in high-voltage regions during AF and high DF sites were located in low voltage regions during AF.
Conclusions: CFAEs and high DF areas during AF do not reflect damaged atrial myocardium as shown by the SR voltage. However, CFAEs and high DF sites may demonstrate different electrophysiologic properties because of different voltage amplitude during AF.

1. Introduction

Catheter-based pulmonary vein isolation (PVI) has become a widely accepted means of treating symptomatic drug-refractory atrial fibrillation (AF) [1]. However, for terminating persistent AF (PerAF), extensive ablation, including ablation at sites of complex fractionated atrial electrograms (CFAEs) and high dominant-frequency (DF) and/or multiple linear ablations may also be necessary [2–5]. CFAEs and/or high DF sites have been shown to be effective targets for AF termination, which suggests the importance of these sites in the maintenance of AF [2,5–8]. CFAEs and high DF sites theoretically represent abnormal substrates; however, sinus rhythm (SR) voltage recorded at the CFAE sites has been shown to be normal [9]. It has also been shown that most CFAE and high DF sites identified during AF do not correspond with high DF sites or low voltage areas identified during SR [10]. In the present study, we compared left atrial (LA) CFAEs and high DF sites identified during AF and LA bipolar voltage recorded during AF and SR by comparing LA bipolar electrograms obtained from both

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high-density mobile-catheter mapping and fixed-position basket-catheter mapping.

2. Material and methods

2.1. Study patients

This study involved 16 consecutive patients (14 men; mean age 58 ± 11 years) scheduled for their first catheter ablation of AF. Eight had paroxysmal AF (PAF), defined as AF lasting <7 days; 8, persistent AF (PerAF), defined as AF lasting ≥ 7 days. Patients with cardiomyopathy, valvular heart disease, or congenital heart disease were excluded from the study. Adequate oral anticoagulation therapy was administered for at least 1 month before the ablation procedure, and all antiarrhythmic drugs were discontinued for at least 5 half-lives before the procedure. Transesophageal and transthoracic echocardiography were performed upon admission, and the following baseline echocardiographic data was obtained: maximum LA volume by the prolate-ellipsoid method and left ventricular ejection fraction by the Teichholz method. The study protocol was approved by the Institutional Review Board of Nihon University and Itabashi Hospital (December 7, 2012; RK-121109-5) and all patients provided written informed consent for their participation.

2.2. Electrophysiologic study

Electrophysiologic evaluation was performed in all patients under conscious sedation using dexmedetomidine, propofol, and fentanyl, as described previously [10,11]. After vascular access was obtained, a single transseptal puncture was performed and intravenous heparin was administered to maintain an activated clotting time of more than 300 s. After two long sheaths (1 SL0 sheath and 1 Agilis sheath; St. Jude Medical, Inc., St. Paul, MN) were inserted into the left atrium via a transseptal puncture, the 3-dimensional (3D) geometry of the left atrium and 4 pulmonary veins (PVs) was reconstructed with the use of an EnSite NavX Classic system (St. Jude Medical, Inc.) and a 20-pole circular mapping catheter with 4-4-4-mm interelectrode spacing (AFocus II catheter, St. Jude Medical, Inc.). We recorded multiple bipolar signals (filter setting: 30–300 Hz) from the AFocus II catheter with the EnSite NavX system classic (St. Jude Medical, Inc.) in 10 patients. We recorded bipolar signals from a 64-pole basket catheter (Constellation, Boston Scientific, Marlborough, MA) placed in the left atrium (Fig. 1A and B) in 6 patients. If the patient was in SR, AF was induced by rapid atrial pacing from the coronary sinus ostium for recording of the CFAEs and DFs at 5 min after AF induction. If the patient was in AF, SR electrograms were recorded after cardioversion.

2.3. Bipolar electrogram recordings

1) AFocus II 20-pole dual ring catheter: Nineteen bipolar electrograms (1–2…19–20) from the 20-pole circular electrodes with 4-mm spacing were recorded simultaneously for a single beat during SR and for 5 seconds during AF, and high-density 3D electroanatomic mapping (>300 signals) of the entire left atrium was performed. Single-beat peak-to-peak bipolar voltages during SR were calculated. Peak-to-peak bipolar voltages during AF were averaged from 5-second recordings at 5 points within each LA segment. The 5 points where the recordings were obtained in each segment during SR and AF were located within 3 mm of each other on the LA 3D map.
2) Constellation 64-pole basket catheter: Owing to the limit on the number of electrodes that can be recorded by the EnSite system classic version, the signals from 1 proximal electrode of each spline of the basket catheter could not be recorded. Thus, 6 bipolar pairs of 7 possible bipolar electrode pairs on each spline (total, 48 bipolar electrograms: 6 pairs $\times$ 8 splines) were analyzed. With the basket catheter in a stable position, the baseline bipolar signals were recorded for a single beat during SR and were averaged over 5 s during the recording of AF from each bipolar electrode of the 48 bipolar electrograms (Fig. 1). The basket catheters used were 38 mm (n=1), 48 mm (n=4), and 60 mm (n=1) in diameter.
3) Bipolar electrogram amplitudes were measured during AF and SR and low voltage was defined as <0.5 mV during AF and <1.0 mV during SR [12].

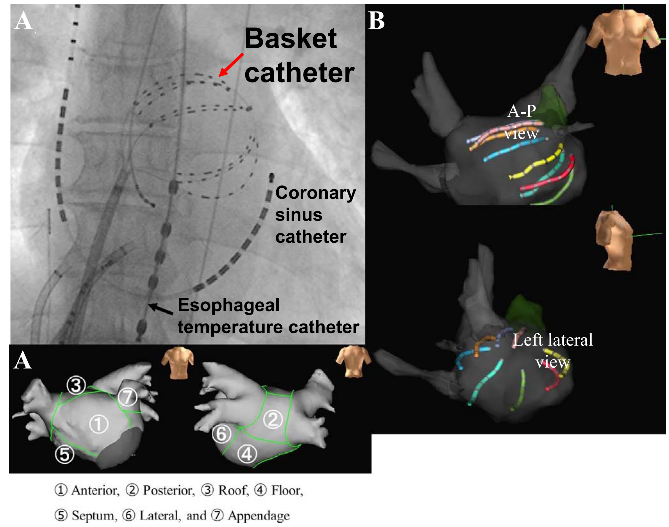

Fig. 1. A. X-ray position of the basket catheter in the left atrium. A-P=antero-posterior. B. Basket catheter position shown on the NavX system. C. Left atrial segmentation. The left atrium was divided into 7 segments and analyzed.

2.4. Time-domain atrial electrogram interval analysis during AF

For the analysis of atrial electrogram intervals, the NavX mapping parameters were set to CFAE-mean, an algorithm was used to determine the average time of the atrial electrogram interval (fractionation intervals; FIs) at each site, and a color map of the FIs was constructed [11,13,14]. The FI was considered the average time between consecutive deflections over a 5-second recording period. Local bipolar activation timing was defined as the peak negative dV/dt point. The settings included a refractory period of 40 ms, peak-to-peak sensitivity between 0.05 mV and 0.1 mV, and duration for each electrogram of <10 ms. Continuous CFAEs were defined as those with a mean FI of <50 ms and variable CFAEs as those with a mean FI of 50–120 ms.

2.5. Fast Fourier transform (FFT) analysis

For FFT analysis, the DF (the highest power frequency) was analyzed by the DF analysis software installed in the NavX mapping system (sampling rate: 1200 Hz; resolution: 0.14 Hz; low-pass filter: 20 Hz; high-pass filter: 1 Hz with a Hamming window function), as reported previously [11,13,14]. Five-second bipolar signals recorded during AF were used for the DF analysis. The DF was defined as the frequency, range of 3–14 Hz, with the maximum power. A high DF site was defined as a site with a frequency of >8 Hz. The regularity index was considered the area within the 0.75-Hz band around the DF divided by the area of the frequencies sampled from 3–14 Hz [15,16]. Signals with a regularity index of <0.2 were excluded from the analysis.

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