Is there a relationship between complex fractionated atrial electrograms recorded during atrial fibrillation and sinus rhythm fractionation?

Laszlo Saghy, MD,* David J. Callans, MD, FHRS,† Fermin Garcia, MD,† David Lin, MD,† Francis E. Marchlinski, MD, FHRS,† Michael Riley, MD, PhD,† Sanjay Dixit, MD, FHRS,† Wendy S. Tzou, MD,† Harris M. Haqqani, MBBS, PhD,† Robert Pap, MD, PhD,* Steven Kim, MS,‡ Edward P. Gerstenfeld, MD†

*From the *Second Department of Medicine, Cardiology Center, University of Szeged, Szeged, Hungary; †Hospital of University of Pennsylvania, Philadelphia, Pennsylvania; ‡St Jude Medical, Minnetonka, Minnesota.*

BACKGROUND Ablation of persistent atrial fibrillation (AF) may require adjunctive methods of substrate modification. Both ablation-targeting complex fractionated atrial electrograms (CFAEs) recorded during AF and fractionated electrograms recorded during sinus rhythm (sinus rhythm fractionation [SRF]) have been described. However, the relationship of CFAEs with SRF is unclear.

METHODS Twenty patients (age 62 ± 9 years, 13 males) with persistent AF and 9 control subjects without organic heart disease or AF (age 36 ± 6 years, 4 males) underwent detailed CFAE and SRF left atrial electroanatomic maps. The overlap in left atrial regions with CFAEs and SRF was compared in the AF population, and the distribution of SRF was compared among patients with AF and normal controls. Propagation maps were analyzed to identify the activation patterns associated with SR fractionation.

RESULTS SRF (338 ± 150 points) and CFAE (418 ± 135 points) regions comprised 29% ± 14% and 25% ± 15% of the left atrial surface area, respectively. There was no significant correlation between SRF and CFAE maps ($r = .2$; P = NS). On comparing patients with AF and controls, no significant difference was found in the distribution of SRF between groups ($P = .74$). Regions of SRF overlapped areas of wave-front collision 75% ± 13% of the time.

CONCLUSIONS (1) There is little overlap between regions of CFAEs during AF and regions of SRF measured in the time domain or the frequency domain, (2) the majority of SRF appears to occur in regions with wave-front collision, (3) the distribution of SRF is similar in patients with AF and normal controls, suggesting that this may not have an important role in AF maintenance and may not be a suitable ablation target.

KEYWORDS Atrial fibrillation; Complex fractionated atrial electrograms; Signal processing

ABBREVIATIONS **AF** = atrial fibrillation; **CFAEs** = complex fractionated atrial electrograms; **CS** = coronary sinus; **FFTr** = fast Fourier transformation ratio; **LA** = left atrium; **PVI** = pulmonary vein isolation; **RA** = right atrium; **SR** = sinus rhythm; **SRF** = sinus rhythm fractionation

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Introduction

Pulmonary vein isolation (PVI) is a well-established and successful method of treatment for paroxysmal atrial fibrillation (AF).[1] However, the success rate using the same strategy has been suboptimal in the population with persistent AF.[2] This observation has led to the development of techniques for modifying the left atrial substrate in the population with persistent AF.

Targeting of complex fractionated atrial electrograms (CFAEs) recorded during AF has been described by Nademanee et al[3] as a stand-alone AF ablation procedure with a high success rate. However, other investigators have not been able to confirm similar efficacy.[4,5] Consequently, it has often been applied as an adjunctive technique to PVI. The mechanism(s) underlying CFAEs observed during AF remains unclear. Numerous experimental and clinical studies suggest that CFAEs can represent potential sources important to the perpetuation of AF,[6–10] while others have demonstrated that this phenomenon may represent passive wave-front collision.[11]

Fractionated electrograms also have been observed in the left atrium (LA) during sinus rhythm (SR) in patients with AF.[12] It has been proposed by Pachon and colleagues[13] that complex electrogram morphologies in SR recorded by frequency domain techniques and termed "AF nests" can serve

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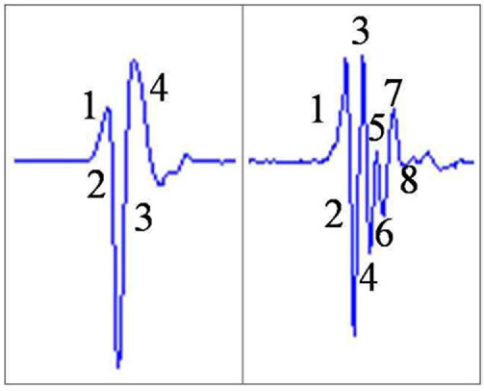

Figure 1 Example of manual calculation of the number of deflections assigned to each atrial electrogram. Each change in slope was incremented to give a total number of deflections. The atrial electrogram on the left is normal appearing and has a fractionation index of 4. The electrogram on the right is fractionated and has a fractionation index of 8.

as a pathologic substrate for AF. Radiofrequency ablation of these sites in SR had a favorable impact on long-term arrhythmia control in both patients with paroxysmal AF and patients with persistent AF in one study.[14]

Since CFAEs recorded during AF and fractionated electrograms recorded during SR (SR fractionation [SRF]) have both been suggested as an ablation target, we sought to elucidate (1) the relationship between the distribution of CFAEs/fragmented areas in the LA during AF and fragmented areas during SR and (2) the mechanism of electrogram fractionation during SR.

Methods

Patients undergoing ablation of persistent AF at the Hospital of the University of Pennsylvania were included in the study. Persistent AF was defined as AF that persisted for >1 month or that typically required cardioversion for AF termination. All patients provided written informed consent. Antiarrhythmic medications were held more than 5 half-lives before the procedure, except amiodarone, which was held for 1 week.

Decapolar catheters were placed in the posterior right atrium (RA) and the coronary sinus (CS). A circular mapping catheter (10-pole, adjustable 15–25-mm Lasso, 6-mm bipole spacing, Biosense-Webster, Diamond Bar, CA) and a 3.5-mm tip-irrigated ablation catheter (Celcius Thermocool, Biosense-Webster, Diamond Bar, CA) were introduced in the LA through double transseptal puncture. Intravenous heparin was infused throughout the procedure to maintain an activated clotting time (ACT) of >350 seconds.

CFAE maps

A 3-dimensional LA geometry was created by using the NavX electroanatomic mapping system (NavX, St Jude Medical, St Paul, MN). After the geometry was created, a detailed bipolar LA CFAE map was acquired during AF by using the circular mapping catheter; undersampled areas were filled in by using the ablation catheter (<10% of all points). The CFAE map was acquired online by using the automated NavX algorithm. At each point, deflections above baseline were automatically detected, and the mean AF fractionation interval was calculated by averaging the intervals between deflections over a 5-second window (refractory period = 50 ms; width =10 ms; sensitivity = 0.05–0.1 mV). The sensitivity was adjusted on a per-patient basis. The lasso catheter was placed distally into a pulmonary vein where no atrial musculature was present, and the detection sensitivity was set just above the level of background noise. Points were included only if they were within 8 mm of the geometry shell, thus minimizing the acquisition of internal or external points that were not in contact with the LA. Regions with a mean fractionation interval of <70 ms were defined as CFAEs. After the procedure, all points were manually overread and signals with significant noise were excluded. All intracardiac signals were acquired at a sampling frequency of 1200 Hz.

SRF map

After DC cardioversion to SR followed by a 5-minute waiting period, a second detailed bipolar LA activation map was acquired in SR, using the same circular mapping catheter. Care was taken to ensure an even distribution of points throughout the left atrial geometry. Offline, premature atrial beats were eliminated. SRF was calculated manually for each electrogram by counting the number of deflections present in each electrogram (Figure 1) and recoding the total number of deflections as the peak-to-peak voltage. In this manner, a color-coded SR "fractionation map" could be displayed (Figure 2A). Normal conduction typically results in 3 deflections of the bipolar electrogram.[14] In order to determine a cutoff for the number of deflections that was considered "abnormal," we determined the 95th percentile of electrogram deflections from our 9 normal control patients, after excluding septal points that have both right and left atrial components. We found that 95% of bipolar electrograms showed ≤5 deflections in our healthy control population; therefore, electrograms with ≥5 deflections were defined as abnormally fragmented.

A frequency domain measure of left atrial SR bipolar electrogram fractionation was also used. The "FFT ratio" (fast Fourier transformation ratio, FFTr) of high (>100 Hz) to total (0–300 Hz) spectral power was automatically computed and displayed on the electroanatomic map by using a customized version of the NavX software (Figure 3). We found that an FFTr cutoff of >20% identified areas of fractionated electrograms during SR.

Left atrial activation maps during SR and CS pacing

The high-density SR maps also allowed a detailed reconstruction of left atrial endocardial activaton. Regions of SRF were outlined on the LA geometry, and activation patterns in regions of SRF were examined to determine the mechanisms of fractionation. We hypothesized that areas of SRF might be related to wave-front collision, and therefore areas