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Correlation of atrial fibrillation cycle length and fractionation is associated with atrial fibrillation free survival

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ABSTRACT

Aims: Fractionation of electrograms in atrial fibrillation (AF) is associated with structural and electrical remodeling. We hypothesized that fractionation can also be associated with the AF cycle length (AFCL). This study was aimed at calculating the mean AFCL to fractionation correlation coefficient (mAFCC) and assessing its association with AF free survival after pulmonary vein isolation (PVI).
Methods: In twenty-eight patients, 15-second electrograms during AF were recorded with a twenty-polar catheter at the left and right atrial appendages. The AFCL was determined manually and the number of activations per second was automatically calculated into a fractionation score. The correlation between AFCL and fractionation was assessed with the mAFCC.
Results: Mean age was 53 ± 8 years and 86% had paroxysmal AF. 64% of patients were AF free after a median follow-up of 5.5 years. Baseline characteristics, mean AFCL and fractionation score were not associated with AF free survival after PVI. The mAFCC assessed at the left atrial appendage predicted long-term AF free survival (area under the curve: 0.871. P = 0.002), but the mAFCC recorded at the right atrial appendage did not (0.690, P = 0.131).
Conclusion: The mean AFCL mAFCC recorded at the left atrial appendage was a significant predictor of long-term AF free survival. Although not a significant predictor of AF free survival, there was a significant association between mAFCC recorded at the right atrial appendage and AF free survival.

1. Introduction

Pulmonary vein isolation (PVI) has become an important treatment modality for "lone" symptomatic atrial fibrillation (AF) [1], although not all patients remain in sinus rhythm, even after multiple PVI attempts [2–6]. Current pathophysiological insights into the mechanisms of AF suggest that this is due to a more extended AF substrate [1]. Several reports have suggested that fractionation of electrograms (EGMs) is a sign of local AF substrate [7,8] and may be associated with AF free survival after PVI. However, other studies reported that fractionation of EGMs is unstable and dynamic [9] and a reduction of AF cycle length (AFCL) was observed prior to a fractionated EGM [10–12]. We hypothesized that in tissue with minimal scar, fractionation may be functional in nature, and the local fractionation score would be correlated to the local AFCL. In contrast, a lack of correlation between AFCL and fractionation may exist in areas with structural remodeling and fibrosis. Therefore, the correlation between AFCL and fractionation may be associated with the atrial scar burden and may predict a lower AF free survival after PVI. The present study was aimed at delineating the AFCL to fractionation correlation and assessing its potential value as a predictor of AF free survival after PVI.

2. Methods

2.1. Patient characteristics

Twenty-eight patients with symptomatic "lone" paroxysmal and persistent AF who were accepted for PVI were included in this study. Written informed consent was obtained from all patients. The local ethics approved the study, which was in accordance with the declaration of Helsinki. Patients with a left atrial dimension of >50 mm were excluded. Class I or III antiarrhythmic drugs of the Vaughan-Williams classification were discontinued >5 half-lives before the start of the procedure, except for amiodarone, which was discontinued at least 3 months prior to the ablation procedure. β-Blockers were allowed. Patients <18 or >65 years and patients with thyroid dysfunction were also excluded. Transesophageal echocardiography was performed routinely 1 h before ablation to assess the interatrial septum, determine

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the right and left ventricular function and valvular abnormalities, and to rule out left atrial thrombus.

2.2. Catheter setup

Electrophysiological study was performed under general anesthesia supervised by a cardiac anesthesiologist using propofol in a patient weight-dependent dose of 2–4 mg/kg/min. A pentapolar catheter (Josephson, Bard, USA) was positioned in the coronary sinus. After a standard transseptal puncture, a bolus of 10,000 IU of heparin was administered to prevent thromboembolism. Additional heparin was administered guided by activated clotting time, measured every 30 min, with a target activated clotting time of 300–350 s. A twentypolar steerable mapping catheter (PentaRay, Biosense Webster, Diamond Bar, CA, USA) was inserted in the left atrium via an 8.5 F sheath. The setup is shown in Fig. 1. The twentypolar mapping catheter had 5 soft radiating splines, with four 1-mm electrodes per spline and a 4–4–4-mm inter-electrode spacing. The electrodes covered an area of approximately 9.6 cm^2.

2.3. Electrophysiological study

Mapping was performed during spontaneous AF in 6 patients and pacing-induced AF in 22 patients. EGMs during AF were recorded at least 2 min after AF induction. EGMs were recorded at the left atrial appendage and at the right atrial appendage, under fluoroscopic guidance. Ten bipolar EGMs were transferred to an amplifier (LabSystem Pro, Bard, USA), amplified with a gain of 500 to 1000, and filtered with a band-pass filter set at 30 to 500 Hz. The sample frequency was 1 kHz.

2.4. AFCL measurement

Data analysis was performed off-line with custom made software based on Matlab (Mathworks, Inc., Natick, Mass) [13]. This software utilizes user-defined settings to determine local activation times and were verified by the operator manually. The chosen settings were: $dV/dT > 0.05$ V/s, amplitude > 0.05 mV and a blanking interval of 120 ms. Previous studies showed a high interobserver correlation of up to 0.99 of manual AFCL determination [14,15]. For all one-second EGM, the mean AFCL was calculated for all 10 bipolar EGMs separately. 15 consecutive seconds of AF EGMs were studied. Per recording site, this yielded 150 mean AFCL values. In Figs. 2 and 3, panel A, the calculation process of the mean AFCL value is displayed.

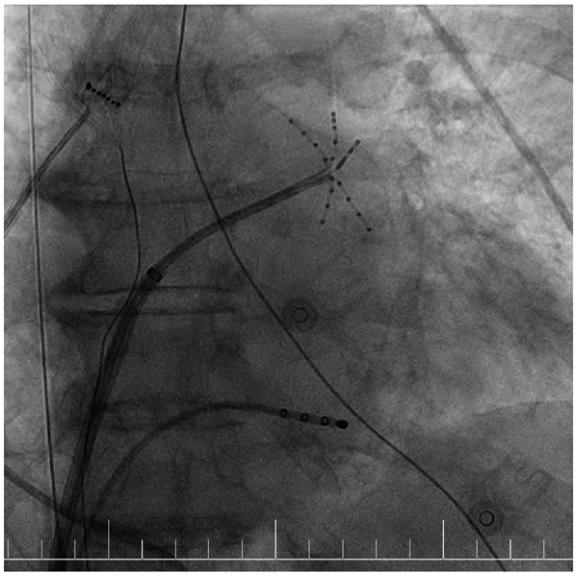

Fig. 1. Fluoroscopic image of electrophysiological setup. A fluoroscopy image with the twentypolar catheter positioned in the left atrial appendage (PA view).

2.5. Fractionation measurement

Commercially available algorithms for defining CFAEs differ between manufacturers and publications. It is usually [7,16] defined as (1) low-voltage multiple potential atrial signals and (2) atrial EGMs with a very short cycle length (70 to 120 ms). However, EGMs can be fractionated without meeting these criteria for CFAE. An EGM is fractionated when it shows more than one deflection per activation cycle length [8] and fractionation is considered to reflect differences in activation time within the recording area of the electrode.

In this study, we aimed at an automatic quantification of fractionation into a fractionation score by using the previously mentioned custom made software based on Matlab and a commonly used algorithm for identification of CFAEs [11,17–21]. The algorithm measured the number of discrete, sharp deflections exceeding −0.015 mV/ms per specified length of time (1 s). The peak-to-peak deflection limit was set just above noise level at 0.05 mV to avoid noise detection while allowing detection of small, fractionated complexes [22]. Blanking interval was set at 8 ms. The fractionation was corrected for the number of main deflections in the corresponding time frame. For all one-second EGMs, the mean fractionation score was calculated for all 10 bipolar EGMs separately. 15 consecutive seconds of AF EGMs were studied. Per recording site, this yielded 150 mean fractionation score values. The settings for fractionation assessment were verified by comparison of automatic to manual fractionation assessment in a subset of patients. The chosen settings gave the best match. In Figs. 2 and 3, panel B, the calculation process for fractionation is displayed.

2.6. Pulmonary vein isolation

All patients underwent conventional point-by-point PVI. A multipolar steerable circular catheter for circumferential pulmonary vein (PV) mapping (Lasso™, Biosense Webster Inc., Diamond Bar, CA, USA) and a radiofrequency (RF) ablation catheter (Thermocool™, Biosense Webster Inc., Diamond Bar, CA, USA) were inserted transseptally into the left atrium. A left atrial electro-anatomical map was created using 3D software (Carto™, Biosense Webster Inc., Diamond Bar, CA, USA). Templates of PV signals were recorded and pacing from the coronary sinus catheter or from the mapping catheter placed in the left atrial appendage was used whenever deemed necessary to distinguish electrical PV potentials from signals generated by activity of other atrial structures. After entering the PV, the circular catheter was positioned as close as possible to the PV ostium. PVI was achieved by delivering RF energy in a point-by-point fashion to the PV antrum creating a circular ablation lesion. RF energy was applied in a temperature-control mode with a temperature setting up to 43 °C. RF energy was applied at 30 W with a flow rate of 15 ml/min or at 40 W with a flow rate of 30 ml/min, depending on the site of ablation. The endpoint of the ablation procedure was PV isolation, as documented by entrance block or dissociation between PV and atrial activation. No adenosine testing was performed. AFCL and fractionation analysis were done after the procedure and thus did not influence the PVI procedure.

2.7. Follow-up

A blanking period of 3 months was defined after PVI. Patients visited the outpatient clinic at 3, 6 and 12 months after PVI. At these times a 24-hour Holter electrocardiogram was made. An attempt was made in all patients to cease AADs after the 3 month visit. After 12 months, additional clinical visits were performed as deemed necessary by the physician. All patients were interviewed telephonically at the end of the study period to assess AF symptoms and AAD use. AF recurrences were defined according to European guidelines [1].