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A High Baseline Electrographic Organization Level Is Predictive of Successful Termination of Persistent Atrial Fibrillation by Catheter Ablation

Andréa Buttu, PhD,[a] Jean-Marc Vesin, PhD,[a] Jérôme Van Zaen, PhD,[a] Pierluigi Ballabeni, PhD,[b] Patrizio Pascale, MD,[c] Andrei Forclaz, MD,[c] Laurence Bisch, MD,[c] Anne Rollin, MD,[d] Philippe Maury, MD,[d] Laurent Roten, MD,[e] Etienne Pruvot, MD[c]

ABSTRACT

OBJECTIVES This study sought to investigate whether the level of organization of electrocardiographic (ECG) signals based on novel indexes is predictive of persistent atrial fibrillation (pAF) termination by catheter ablation (CA).

BACKGROUND Whether the level of ECG organization in pAF is correlated with the restoration of sinus rhythm by CA remains unknown.

METHODS Thirty consecutive patients who underwent stepwise CA for pAF (sustained duration 19 $\pm$ 11 months) were included in the study (derivation cohort). ECG lead V_6 was placed on the patients' back (V_{6b}) to improve left atrial (LA) recording. Two novel ECG indexes were computed using an adaptive harmonic frequency tracking scheme: 1) the adaptive organization index (AOI), which quantifies the cyclicity of AF harmonic oscillations; and 2) the adaptive phase index (API), which quantifies the phase coupling between the harmonic components. Index cutoff values predictive of procedural AF termination were then tested on a validation cohort of 8 consecutive patients.

RESULTS In the derivation cohort, CA terminated AF in 21 patients within the LA (70%; left-terminated [LT] group), whereas CA did not terminate AF in 9 patients (30%; non–left-terminated [NLT] group). LT patients displayed a higher ECG organization level at baseline than the NLT patients, with the best separation achieved by AOI and API computed on lead V_1 (area under the curve [AUC] = 0.94 and AUC = 0.88, respectively; $p < 0.05$) and API on lead V_{6b} (AUC = 0.83; $p < 0.05$). Similar results were obtained for both AOI and API in the validation cohort.

CONCLUSIONS Patients in whom pAF terminated within the LA exhibited a higher level of atrial ECG organization, which was suggestive of a limited number of LA drivers than that of patients in whom the pAF could not be terminated by CA. (J Am Coll Cardiol EP 2016;2:746–55) © 2016 by the American College of Cardiology Foundation.

In persistent AF (pAF), significant electrical and structural remodeling of the atria provides diffuse substrates for AF perpetuation (1-3). The success of pulmonary vein isolation appears to be limited in pAF (4). Hence, additional strategies have been advocated, such as linear lesions (5) and/or ablation of complex fractionated electrograms (6). Several indexes have been developed in an attempt to determine the level of AF complexity predictive of AF termination by catheter ablation (CA), however, with limited success (7-10). Using a power spectral estimation of atrial electrographic and electrograms

From the [a]Applied Signal Processing Group, Lausanne Federal Institute of Technology, Lausanne, Switzerland; [b]Clinical Research Centre and Institute of Social and Preventive Medicine, Lausanne University Hospital, Lausanne, Switzerland; [c]Service of Cardiology, Lausanne University Hospital, Lausanne, Switzerland; [d]Service of Cardiology, Centre Universitaire de Rangueuil, Toulouse, France; and the [e]Department of Cardiology, Inselspital, Bern University Hospital, Bern, Switzerland. This study was supported by grants SNF 205321-129876/1 and 146811/1 from the Swiss National Science Foundation. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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(EGMs) based on fast-Fourier transforms (FFTs), several investigators showed a shift toward higher dominant frequency (DF) values with broader spectral distribution across the left atrium (LA) with AF sustainability. However, FFT assumes that the signal under consideration is stationary, that is, that the period of the oscillations is constant over time, which may not be the case in pAF (11,12). To overcome this limitation, we used an adaptive harmonic frequency tracking [HFT] scheme based on complex oscillators specifically designed to extract periodic components. We hypothesized that the level of atrial electrocardiographic (ECG) signal complexity is correlated with the atrial remodeling stage in pAF as determined by termination using a stepwise catheter ablation (step-CA) approach.

METHODS

ELECTROPHYSIOLOGICAL STUDY. More details are available in the Online Appendix. A 3.5-mm, cooled-tip catheter for mapping and ablation (Navistar Thermocool, Biosense Webster, Irwindale, California) was introduced via the right femoral vein. ECG chest lead V_6 was placed on the back (lead V_{6b}) of the patients to improve the recording of LA activity (9,13,14). Surface ECG and intracardiac EGMs were continuously monitored and sampled at 2 kHz (Axiom Sensis XP, Siemens, Berlin, Germany) for off-line analysis.

ABLATION STRATEGY. Termination of pAF was defined as the organization of AF into atrial tachycardia (AT) or into sinus rhythm (SR) during step-CA. Nonterminated pAFs were electrically cardioverted. See the Online Appendix for details of index and redo ablations.

PATIENT POPULATION. The derivation cohort consisted of 30 consecutive patients referred for a first ablation (mean age, 61 ± 7 years) suffering from AF for 6 ± 4 years, sustained for 19 ± 11 months before ablation and resistant to pharmacological and electrical cardioversion. **Table 1** reports the clinical characteristics of the study population. Based on the clinical outcome of the procedure, the derivation cohort was divided into 2 groups.

Group 1 (n = 21) consisted of left-terminated (LT) patients in whom pAF was terminated into SR/AT by step-CA. Group 2 (n = 9) consisted of non–left-terminated (NLT) patients in whom step-CA failed to terminate pAF.

Clinical follow-up was performed at scheduled visits at 3, 6, 12, 18, and 24 months, then every year, and included echocardiographic evaluation, ECG, and 48-h Holter recordings. Recurrence was defined as AF or atrial tachyarrhythmia lasting >30 s.

SIGNAL PROCESSING OF ECG SIGNALS. Cancellation of ventricular activity was performed to ensure the reliability of surface ECG analysis during pAF. QRST waves were canceled from ECG recordings using the single-beat method (15). More details are provided in the Online Appendix.

The extraction of the fundamental component and its first harmonic from the atrial ECG was performed using a novel scheme (the HFT) based on an adaptive algorithm. The HFT is based on time-varying band-pass filters for the fundamental and each harmonic component. For each filter, the transfer function is defined as follows:

$$H(z; k \cdot w[n]) = \frac{1-\beta}{1-\beta e^{jkw[n]}z^{-1}}$$

where j is the imaginary unit; $k = 1, \ldots, K$ is the kth harmonic; z is the variable from the Z-transform; β $(0 \ll \beta < 1)$ controls the filter bandwidth; and $w[n]$ is the instantaneous angular frequency estimate that controls the central frequency (by definition $w[n] = 2\pi f[n]$, $f[n]$ being the instantaneous frequency). The filter has unit gain and zero phase at $w[n]$, which is essential for measuring the phase coupling between the harmonic components. The filtered outputs are given by:

$$y_k[n] = \beta e^{jkw[n]} y_k[n-1] + (1-\beta)x[n], \quad k = 1, \ldots, K$$

where $x[n]$ and $y_k[n]$ are the input and output signals. From each of these extracted harmonic components, an instantaneous estimate of the fundamental angular frequency is computed using the following equations:

$$Q_k[n] = \delta Q_k[n-1] + (1-\delta) y_k[n] \overline{y}_k[n-1]$$

$$w_k[n+1] = \frac{\arg\{Q_k[n]\}}{k}, \quad k = 1, \ldots, K$$

where $Q_k[n]$ is an internal variable; δ $(0 \ll \delta < 1)$ is a forgetting factor controlling the convergence rate; and the upper bar denotes complex conjugation. This adaptive scheme extracts separately the oscillations of the fundamental and its harmonics in a given signal, and estimates their instantaneous frequencies.

A detailed summary as well as an illustration (Online Video 1) of the algorithm are provided in the Online Appendix.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
AFCL = atrial fibrillation cycle length
AOI = adaptive organization index
API = adaptive phase index
AT = atrial tachycardia
AUC = area under the curve
CI = confidence intervals
DF = dominant frequency
EGM = electrogram
FFT = fast-Fourier transform
f-waves = fibrillatory waves
HFT = harmonic frequency tracker
LA = left atrium
LT = left terminated
NLT = non–left-terminated
OI = organization index
OR = odds ratio
pAF = persistent atrial fibrillation
PC = phase coupling
RA = right atrium
ROC = receiver-operating characteristic
step-CA = stepwise catheter ablation
SR = sinus rhythm