Measures of Right Atrial Organization as a Means to Select Candidates for Sinus Rhythm Restoration by Catheter Ablation

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Abstract

Stepwise catheter ablation (step-CA) can terminate long-standing persistent atrial fibrillation (LS-pAF) within the left atrium (LA) or may require additional right atrial (RA) ablation. Intracardiac organization indices such as AF cycle length (AFCL) have been used to track the efficiency of step-CA, but predictive parameters of procedural success are lacking. In this study, we hypothesized that the oscillations of time intervals between consecutive AF wavefronts reflect the underlying AF dynamic. We report a new method for quantifying the temporal variability of atrial activation wavefronts (VAW). Our results suggest that the mean and variance of the oscillations around the mean AFCL computed before any ablation can identify patients whose LS-pAF will terminate within the left atrium. These findings are indicative of a higher baseline organization in AF terminated within the left atrium.

1. Introduction

Atrial fibrillation (AF) is associated with an increased risk of morbidity and mortality [1]. Most AF triggers are located within the pulmonary veins (PV) that can be isolated by catheter ablation (CA) [2]. Sites with continuous high frequency activities, described as complex fractionated electrograms (CFAEs [3]), and regions showing structural discontinuities within the left atrium (LA) are believed to be involved in AF maintenance [3]. In long-standing persistent AF (LS-pAF), CFAEs ablation throughout the atria may restore sinus rhythm (SR) [3], while others reported the incremental benefit of linear ablations over PV isolation (PVI) using a stepwise approach [4]. Hence, stepwise CA (step-CA) has become the treatment of choice for the termination of LS-pAF [5]. The success rate of step-CA, however, appears limited as the amount of ablation and whether right atrial (RA) lesions are required to achieve procedural AF termination remain unknown yet. There is therefore a strong interest in predicting the procedural outcome from baseline recordings (i.e. before any ablation) of step-CA for patients with LS-pAF.

Conflicting results were reported regarding the ability of intracardiac AF cycle length (AFCL) to assess AF organization before step-CA, [6, 7, 8]. For instance, baseline AFCL was found significantly longer in patients in whom LS-pAF terminated during step-CA [6, 7], while in LS-pAF persisting despite PVI the baseline AFCL did not differ between patients whose LS-pAF did and did not terminate [8].

In this study, we hypothesized that the temporal variability of atrial activation wavefronts (VAW) around the mean AFCL before any ablation may help identify patients whose LS-pAF will terminate during step-CA. This approach evaluates the oscillations of time intervals between consecutive AF wavefronts similarly to that of heart rate variability analysis [9].

2. Methods

2.1. Patients and data acquisition

Electrophysiological study. All patients had effective anticoagulation therapy for > 1 month. All antiarrhythmic drugs, except amiodarone and beta-blockers, were discontinued for ≥ 5 half-lives before the procedure performed under general anesthesia. The following catheters were introduced via the right femoral vein: 1) a 3.5 mm cooled-tip ablation catheter for mapping and ablation, 2) a quadripolar catheter into the RA appendage (RAA), and 3) a circumferential duodecapolar Lasso catheter within the LA appendage (LAA). Endocardial EGMs were continuously monitored and recorded for off-line analysis at 2-kHz sampling rate (Axiom Sensis XP, Siemens).

Ablation protocol. Step-CA (Fig. 1) consisted in PVI, followed by CFAEs and LA linear ablations (roof and mitral isthmus). RA CFAEs and cavotricuspid isthmus linear ablation were performed if AF was not terminated within the LA. At the end of the procedure, following AF termination or electrical cardioversion, PVI and bidirectional conduction blocks across the lines were checked and completed when needed.

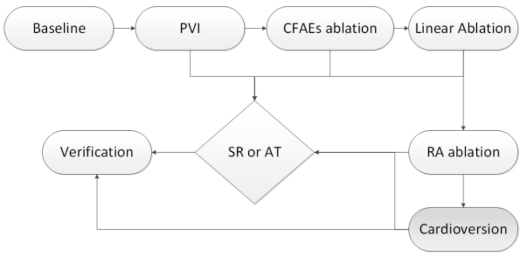

Figure 1. Step-CA protocol.

Procedural endpoint. The study endpoint was reached when AF was terminated into SR or atrial tachycardia (AT). Non terminated AF were cardioverted electrically.

Study population. The study group consisted in 30 consecutive patients (61±7 years) with LS-pAF (AF duration 6±4 years, sustained for 19±11 months, and resistant to pharmacological and electrical cardioversion). Based on the clinical outcome of the procedure, the study population was divided into two groups:

- *Left terminated (LT):* patients in whom AF was terminated into SR/AT during LA ablation.
- *Right terminated/Not terminated (RT/NT):* patients who required RA ablation including those terminated within the RA (RT) or not terminated (NT).

2.2. Signal processing

Bipolar signals from the RAA and LAA were acquired simultaneously at baseline for a duration of 20-sec. Fig. 2 illustrates the signal processing steps:

1. **Detection of local activation time (LAT).** LAT was defined as the time index of the maximum positive peak of each activation wave detected using sliding windows of 150 ms. False detections were removed using temporal and amplitude thresholding. In Fig. 2 panel A1, a 20-sec epoch from the RAA in an LT patient is shown in blue with its detected LATs (red dots). An excerpt of 2 seconds is shown in panel A2.

2. **AFCL.** The AFCL was computed as the mean difference in LATs (Fig. 2 panel B, green horizontal line).

3. **Variability of Atrial Activation Wavefronts (VAW).** Let N be the total number of LATs in a given signal. We set δ_k (Fig. 2 panel A2) as the time difference between two consecutive LAT:

$$\delta_k = LAT_{k+1} - LAT_k$$

k = 1, ..., N-1. We defined the set of data points as (Fig. 2 panel B, pink diamonds):

$$\begin{cases} x_k = LAT_k + \frac{\delta_k}{2} \\ y_k = \delta_k \end{cases} \quad (1)$$

The VAW signal is defined as the cubic interpolation of these data points at a regular sampling frequency of 20 Hz (Fig. 2 panel B, black signal). From equation (1), the mean VAW corresponds to the mean AFCL. In order to characterize the VAW, the VAW power spectrum density (PSD) was estimated using Welch's method (segment length of 512 samples, 50% overlap). Let L be the number of PSD estimates, *f* and *p* the vector of frequency and power spectral density estimates. Two indices were computed:

i. The mean frequency μ_F:

$$\mu_F = \frac{\sum_{i=1}^{L} p_i f_i}{\sum_{i=1}^{L} p_i} \; [Hz] \quad (2)$$

ii. The variance σ_F:

$$\sigma_F = \frac{\sum_{i=1}^{L} p_i (f_i - \mu_F)^2}{\sum_{i=1}^{L} p_i} \; [Hz^2] \quad (3)$$

From equation (2), μ_F quantifies the mean frequency at which the AFCL oscillates. Low values of μ_F are indicative of a slower temporal variability of LATs. From equation (3), σ_F characterizes the spread of μ_F. Low values of σ_F is indicative of a stable μ_F, i.e. a more regular variability; conversely, large σ_F values reflect a more erratic variability.

The AFCL, μ_F and σ_F were computed on all 20-sec epochs of the LAA and RAA recordings, and averaged for each subject. This resulted in one value for each measure, subject and intracardiac location.

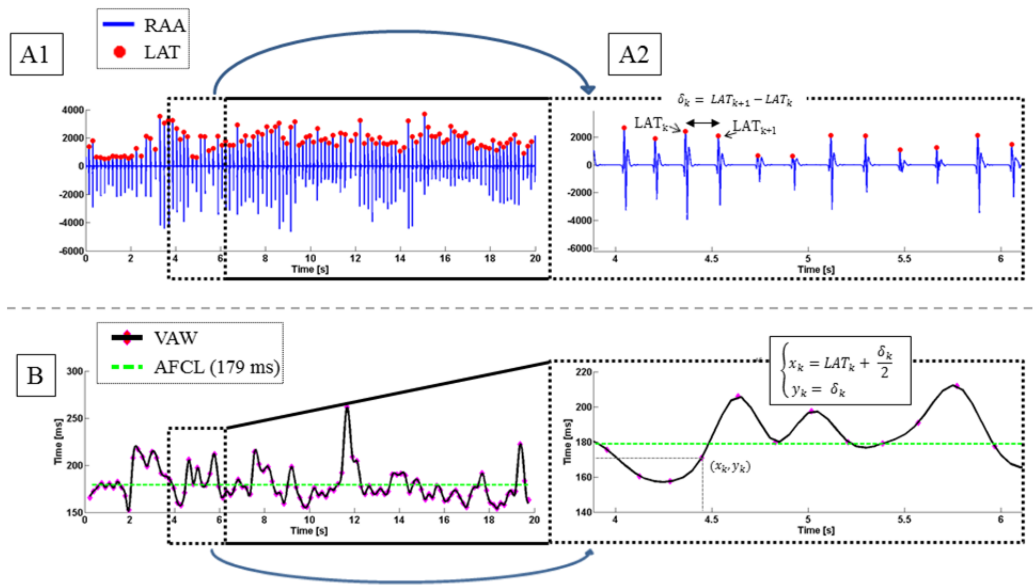

Figure 2. Signal processing steps. Panel A1: 20-sec epoch acquired within the RAA (blue line) and the LATs (red dots). Panel A2: an excerpt of 2 seconds. Panel B: the RAA VAW (black pink dotted line) with the corresponding AFCL (green line)

3. Results

Study population. Twenty one (70%) patients were terminated during LA ablation (LT). Nine (30%) patients required further RA ablation among whom three (10%) were RT and six (20%) were not (NT).

AF organization measurements. Fig. 3 displays representative examples of normalized VAW PSD from an LT (blue solid line) and an NT patient (red dashed line). The PSD estimate for the LT patient is mostly concentrated below 2 Hz with low values for μ_F and σ_F (0.66 Hz and 0.32 Hz^2 respectively) as opposed to the NT patient displaying a widespread PSD distribution with higher μ_F and larger σ_F (1.26 Hz and 0.87 Hz^2 respectively).

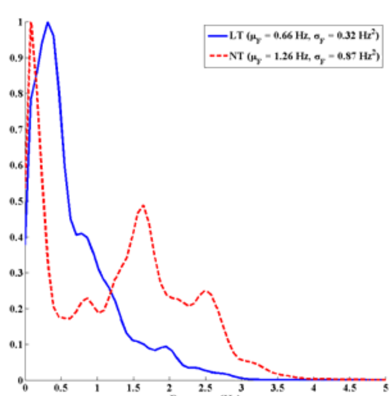

Figure 3. Representative examples of VAW PSD of an LT patient (blue solid line) and an NT patient (red dashed line). Note the higher AF organization for the LT patient.

Clinical results. Fig. 4 reports box plots of the organization indices for the RAA (panel A) and the LAA (panel B). Before ablation, LT patients displayed significantly longer bi-atrial AFCL both for LAA and RAA. Likewise, LT patients displayed significantly smaller RAA and LAA μ_F, and RAA σ_F values compared to RT/NT patients.

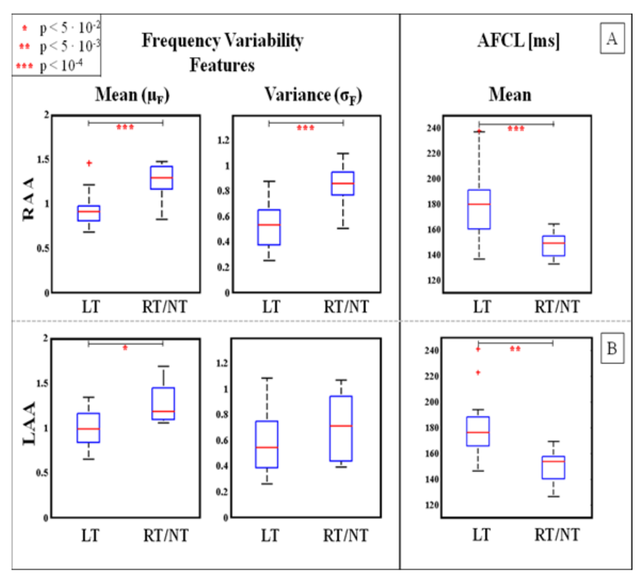

Figure 4. Distribution of measures of AF organization. Panel A: RAA. Panel B: LAA.

4. Discussion and conclusion

Divergent results were reported regarding the ability of intracardiac AFCL to predict the procedural outcome of step-CA [7, 8]. These studies, however, included persistent AF of variable duration with assessment of AFCL at different atrial locations. It has recently been shown that patients with long baseline AFCL measured within the LAA and RAA have a better procedural outcome compared to patients with short value [7]. After the exclusion of AF of shorter duration, the AFCL measured within the coronary sinus failed to predict AF termination in patients whose AF continued despite PVI [8]. In our study, however, we found that the AFCL was significantly longer in both appendages in LT compared to NT/RT patients. No definite explanation can be given for these discrepancies but one may hypothesize that the AFCL from the CS reflects the composite activation of neighboring structures including the CS itself and the LA [10].

In this study, we proposed to extend the analysis of the AFCL by measuring its variability using new indices based on the VAW. These indices characterized the mean frequency (μ_F) and variance (σ_F) of the oscillations around the mean AFCL. We observed that patients whose LS-pAF terminated within the LA displayed a lower RA VAW suggestive of a higher temporal stability of the activation wavefronts within the RA. In contrast, within the LAA, all patients displayed similar VAW, which is indicative of similar timing of activation wavefronts. A recent study has proposed an index of AFCL stability based on the histogram of the inverse of intervals between consecutive atrial activation wavefronts [11]. The authors observed that AF terminated into SR displayed higher AFCL stability than that of unterminated AF during step-CA ablation. Our results extend these recent findings by showing that the frequency of variation and range of variability of atrial activation wavefronts offer potential discriminative values that deserve further clinical validation.

In conclusion, our results suggest that biatrial AFCL, mean VAW, and RAA VAW variance may be used to select best LSp-AF candidates for step-CA ablation.

Acknowledgements

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References

[1] Stewart S, et al. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002; 113: 359 – 364.

[2] Haissaguerre M, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998; 339: 659 – 666.

[3] Nademanee K, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the elctrophysiologic substrate. J Am Coll Cardiol 2004; 43: 2044-2053.

[4] Haissaguerre M, et al. Changes in atrial fibrillation cycle length and inducibility during catheter ablation and their relation to outcome. Ciculation 2004; 109: 3007-3013.

[5] Fuster V, et al. 2011 guidelines for the management of patients with atrial fibrillation: a report of the American college of cardiology foundation/American heart association task force on practice guidelines. Circulation 2011; 123:e269-e367.

[6] O'Neill MD, et al. The stepwise approach for chronic atrial fibrillation – Evidence for a cumulative effect. J Interv Card Electrophysiol 2006; 16: 153-167.

[7] Hocini M, et al. Disparate evolution of right and left atrial rate during ablation of long-lasting persistent atrial fibrillation. J am Coll Cardiol 2010; 55: 1007-1016.

[8] Forclaz A, et al. Early temporal and spatial regularization of persistent atrial fibrillation predicts termination and arrhythmia-free outcome. Heart Rhythm 2011; 8: 1374-1382.

[9] Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology. Heart Rate Variability – Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 1996; 17: 354-381.

[10] Pascale P, et al. Pattern and timing of the coronary sinus activation to guide rapid diagnosis of atrial tachycardia after atrial fibrillation ablation. Circ Arrhythm Electrophysiol 2013; 3: 481-490.

[11] DiMarco LY, et al. Characteristics of atrial fibrillation cycle length predict restoration of sinus rhythm by catheter ablation. Heart Rhythm 2013; 10: 1303-1310.

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